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Dossier de Validation des acquis et de l'expérience

L'aphasie en phase aiguë de l'accident vasculaire cérébral : Nouvelles données, outils d'évaluation et perspectives.

Deuxième partie : Retour d'expérience de recherche

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Sommaire

Introduction :

L’accident vasculaire cérébral (AVC) constitue un enjeu de santé publique majeur. En effet, environ 150 000 AVC sont recensés en France chaque année. Ils représentent la troisième cause de mortalité chez l’homme, la deuxième chez la femme et la première cause de handicap acquis de l’adulte. Sachant que la tendance actuelle est à l’augmentation en raison du vieillissement de la population, la prévention et la prise en charge des AVC est une thématique nationale pour les années 2010 à 2014 (Plan d’actions national ministériel « AVC 2010 – 2014 » ; http://www.has-sante.fr) (1, 2, 3).

La prise en charge immédiate est la plus efficace sur le plan de la survie et de la limitation des séquelles. La création des unités de soins intensifs neuro- vasculaires (USINV) a permis de diminuer la durée de séjour hospitalier, la gravité des séquelles ainsi que la mortalité. Le bénéfice de ces unités sur la morbidité, la mortalité et la récupération est établi sur la base de nombreuses études randomisées (4, 5, 6).

L’utilisation de la fibrinolyse a également modifié la prise en charge très précoce des patients avec AVC ischémique : la thrombolyse peut être pratiquée jusqu’à 4 h 30 après le début des symptômes, et permet de désagréger le thrombus à l’origine de l’accident vasculaire. Les fibrinolytiques permettent une diminution de 20 % du nombre des patients handicapés dans les suites d'un AVC ischémique, une baisse de 30 % de la mortalité et un taux de guérison de 40 % (vs 25 % sans fibrinolyse).

L’aphasie est une des séquelles particulièrement invalidantes des AVC. L’aphasie est un trouble du langage qui affecte l’expression et/ou la compréhension, dans la modalité orale comme écrite. Le patient est alors incapable d’utiliser le langage pour communiquer. L’aphasie est liée à une atteinte de l’hémisphère dominant, c’est-à-dire l’hémisphère gauche pour les droitiers ainsi que pour 70 % des gauchers. Elle concerne entre 15 et 55 % des patients en phase aiguë (7, 8, 9, 10) et leur fréquence est probablement plus élevée à la phase très précoce (premiers jours suivant l’AVC). Ces troubles du langage semblent d’autant plus fréquents que les patients sont âgés, de sexe féminin, et que l’accident est d’origine cardio- embolique (11).

Si les troubles phasiques tendent à régresser naturellement dans la première année, 50% des patients gardent des séquelles 18 mois après l’AVC (10,12,13,14). Leur persistance à distance de l’AVC constitue un facteur indépendant d’altération de la qualité de vie qui va au- delà du déficit de langage proprement dit (15), s’associant à des symptômes dépressifs, un retrait social et une moindre probabilité de reprendre une activité professionnelle (12,15,16, 17) A ce jour, seule la gravité initiale est prédictive du devenir des troubles du langage à long terme; aucun autre facteur pronostic de récupération n’est identifié (7, 10)

Pendant les premières semaines suivant l’AVC, la plasticité cérébrale permet de nombreux changements dans l’organisation du cerveau. La récupération des fonctions du langage est liée à différents facteurs : la taille de la lésion, sa localisation, sa nature ischémique ou hémorragique, le niveau antérieur du patient, l’implication de l’entourage. La prise en charge précoce et intensive de l’aphasie permet de diminuer les séquelles langagières et d’améliorer considérablement la communication des patients par la mise en jeu synergique de la réorganisation neuronale précoce (17).

Orthophoniste depuis 20 ans dans le service de neurologie du CHU de Bicêtre, et depuis 2007 dans son USINV, je me suis particulièrement intéressée aux aspects suivants :

- Quelle est l'évolution et la typologie des aphasies en phase très aigue des AVC, c'est à dire entre J0 et J3 ? Se présentent-elles différemment de ce qui est connu et déjà publié en phase moins aiguë?

- Comment évaluer très précocement les déficits de langage, en particulier lors d'une alerte thrombolyse, afin d'apporter des précisions capitales sur l'importance du déficit du patient, et son éligibilité au traitement fibrinolytique ?

- L'évolution de l'aphasie pendant l'hospitalisation en USINV suit-elle la même courbe, grâce à la prise en charge très précoce, que les autres déficits, tels que les troubles moteurs ?

A travers plusieurs travaux de recherche, j'ai pu tenter de répondre à ces questionnements. Dans ce document, je présente plus en détail ces trois axes d'investigation, mais il doit être signalé que cela ne recouvre pas tous mes champs de recherche.

En effet, je me suis intéressée par ailleurs à d'autres sujets, tels que la dysarthrie dans les pathologies du mouvement, le langage dans l'épilepsie, et la déglutition en phase aiguë de l'AVC. Au total, sur mes 20 ans de carrière hospitalière, j'ai produit 20 publications dans des revues avec comité de lecture ; 18 en anglais et 2 en français. Cinq de ces publications ont été acceptées dans des revues avec facteur d'impact (impact factor, IF) au-dessus de 5, 11 dans des revues avec IF entre 3 et 5. Quant à mon rôle, j'ai été le premier auteur de 5 publications et je suis le dernier auteur d'un article en cours d'écriture. Mon facteur d'index cumulé est 43,85, et mon h-index Google scholar est 9.

La suite de ce document se centre sur les trois lignes de recherche évoquées précédemment.

Evolution des aphasies en phase très aigue des AVC

Les études concernant la typologie des aphasies dans les AVC sont peu nombreuses, et leurs résultats sont hétérogènes, notamment en raison des disparités dans la méthodologie et le moment de l'évaluation du langage.

Sur la base d'une classification en trois groupes de 1500 aphasiques en suite d'AVC, il a été observé 38 % d'aphasies de type mixte, 37 % d'aphasies à prédominance expressive et 25 % à prédominance sensorielle, incluant un nombre conséquent d'aphasies ne s'expliquant pas par les corrélations clinico-radiologiques classiques (26 %) (11). D'autres études ont rapporté des constatations plus fines : à partir de 207 patients, Godefroy et al. (2002) (9) décrivaient une prédominance d'aphasies sévères et de type global ou « inclassables » (50 %), alors que les autres types d'aphasies « classiques » (Wernicke, Broca, transcorticales, sous-corticales) étaient étonnamment minoritaires lorsque les patients étaient explorés en phase aigue¨(en moyenne à J10 dans cette étude) (9). A partir d'une étude prospective de 270 patients aphasiques consécutifs, examinés lors du premier mois après l'AVC, Pedersen et al. (2004) (10) rapportaient environ 32 % d'aphasies globales, 25 % d'anomiques, 16 % de type Wernicke, 12 % de type Broca, 7 % de transcorticales sensorielles et 2 % de transcorticales motrices, et enfin 5 % de type conduction. L'hétérogénéité des résultats de ces études est en partie expliquée par l' amélioration rapides des symptômes, caractéristique de l'histoire naturelle de ces aphasies, et observée chez près d'un patient sur deux dès J10 (7).

Dans ce projet, je me suis concentrée sur un type d'aphasie particulier, les **aphasies transcorticales dans le cadre des infarctus jonctionnels.** Au cours de ma pratique clinique j'ai constaté que les patients avec un accident vasculaire cérébral dans le même territoire jonctionnel, présentaient le même type d'aphasie avec des profils évolutifs similaires. Nous avons donc effectué une recherche exhaustive dans la littérature, et constaté que ce pattern précis n'avait jamais été décrit.

Fiche de recherche :
Rôle : **investigateur principal.** Rédaction du protocole pour obtention de l'accord du comité d'éthique de Bicêtre, administration du protocole, rédaction et soumission de l'article.
Equipe de recherche : Dr C. Denier (INSERM U788), Dr E. Roze (INSERM U952, CNRS UMR7224 UPMC Paris 6), Pr D. Adams, Pr D. Ducreux, Dr C. Cauquil-Michon .
Nombre de patients : 8
Type de recherche : Etude de cas cliniques.
Site : CHU Bicêtre, service de Neurologie adulte, USINV

Méthodes :

Nous avons recruté des patients consécutivement sur un an, ceux-ci présentant un accident vasculaire cérébral de la jonction de deux artères. Le but de l'étude était de déterminer un pattern aphasiologique commun à ces patients et lié à leurs localisations lésionnelles. Nous avons évalué le langage le jour de l'accident, à 8 jours de l'accident et à 3 mois lors de la consultation systématique de suivi.

Résultats :

Tous les patients présentent le même type d'aphasie à l'entrée, et évoluent favorablement selon un schéma précis en fonction des artères concernées. Cette recherche a permis de déterminer un profil aphasiologique et un type d'évolution dans le cadre des AVC jonctionnels gauches. Ce profil typique de trouble du langage peut donc s'inscrire dans une démarche diagnostique en phase aigue : face à un patient présentant ce profil, il faut rechercher ce type de localisation lors de l'imagerie. De plus, tous les patients ayant retrouvé leur niveau de langage antérieur à 3 mois, nous avons également apporté des éléments en faveur d'un bon pronostic dans ce type d'accident.

Aphasia in border-zone infarcts has a specific initial pattern and good long-term prognosis

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Background: While border-zone infarcts (BZI) account for about 10% of strokes, studies on related aphasia are infrequent. The aim of this work was to redefine specifically their early clinical pattern and evolution.
Methods: We prospectively studied consecutive patients referred to our stroke unit within a 2-year period. Cases of aphasia in right-handed patients associated with a MRI confirmed left-sided hemispheric BZI were included. These patients had a standardized language examination in the first 48 h, at discharge from stroke unit and between 6 and 18 months later.
Results: Eight patients were included. Three had anterior (MCA/ACA), two posterior (MCA/PCA), two both anterior and posterior, and one bilateral BZI. All our patients initially presented transcortical mixed aphasia, characterized by comprehension and naming difficulties associated with preserved repetition. In all patients, aphasia rapidly improved. It fully recovered within a few days in three patients. Initial improvement was marked, although incomplete in the five remaining patients: their aphasias specifically evolved according to the stroke location toward transcortical motor aphasia for the three patients with anterior BZI and transcortical sensory aphasia for the two patients with posterior BZI. All patients made a full language recovery within 18 months after stroke.
Conclusions: We report a specific aphasic pattern associated with hemispheric BZI, including an excellent long-term outcome. These findings appear relevant to (i) clinically suspect BZI and (ii) plan rehabilitation and inform the patient and his family of likelihood of full language recovery.

Introduction

Aphasia is one of the most common symptoms in acute cerebral infarction, occurring in 16–38% of cases [1,2]. Impairing communication, aphasia is associated with deleterious effects on social activities and can induce depression [1,2]. Although aphasia usually improves during the first year after stroke, the outcome of language function cannot be predicted, with 32–50% of patients still suffering from aphasia 6 months after stroke [1–3]. Moreover, the recovery of aphasia may for unknown reasons differ amongst patients despite similar age, clinical presentation and MRI findings. This wide variability in recovery makes individual prognosis difficult to predict [1,2]. To date, the severity of aphasia and initial NIHSS score stroke are the only independent strong predictors of long-term dependence[1–6]. No other prognosis factor has been identified: gender, age, as well as aphasia subtype were non-significant in previously published studies [1–3].

Border-zone hemispheric cerebral infarcts (BZI) account for about 10% of ischaemic strokes [7]. Little attention has so far been paid to aphasia-related BZI. The few series devoted to this topic found that most aphasic patients with anterior cerebral artery (ACA)/middle cerebral artery (MCA) ('anterior') BZI have transcortical motor aphasia (TMoA) and those with MCA/posterior cerebral artery (PCA) ('posterior') BZI have transcortical sensory aphasia (TSeA) [8,9]. Besides these classical patterns, patients have been also reported

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with other types of aphasia including Wernicke aphasia in posterior BZI, anomia, mutism or transcortical mixed aphasia in anterior or posterior BZI [8,10,11]. These studies were often based on CT imaging and often lacked details on speech evaluation, on patterns of recovery and on long-term outcome [8,9,12].

In order to describe the initial clinical pattern, early course and final outcome of aphasia in border-zone infarctions (BZI), we prospectively studied consecutive right-handed patients with a left-sided hemispheric MRI confirmed BZI using a standardized language examination.

Patients and methods

Patients

Our prospective stroke cohort includes 944 consecutive patients admitted in our stroke unit for suspected stroke or TIA between January 2008 and December 2009. Initial diagnostic studies systematically included routine laboratory work-up and cerebral MRI within the first 48 h after admission (on 1.5 Tesla Siemens MRI, according to a 'MRI stroke protocol' including: T1-, diffusion-weighted (DW), FLAIR, gradient-echo sequences, time of flight (TOF) and magnetic resonance angiography of the supraaortic trunk (MRA SAT). Patient's characteristics were routinely entered in our database. Amongst this cohort, stroke mimics were diagnosed in 284 patients (including mostly seizures/postictal paresis, hypoglycemias, complicated migraines, conversion disorders, and various myelopathies or brain tumors). Others, 660 patients presented acute cerebro-vascular diseases including 414 MRI confirmed cerebral infarctions; the 246 remaining patients presented transient ischaemic attacks and intracerebral hematomas. The study was approved by the ethics committee of Pitié-Salpêtrière Hospital, Paris, and all patients gave their informed consent.

Methods

Patients were included in this study if they were right-handed French native speakers and presented an aphasia associated with a DWI MRI-confirmed acute hemispheric infarction located at the border zone between two adjacent vascular territories according to the mapping guidelines described by Damasio [8,13]. All brain MRI were independently reread by two of us (R.S-S and D.D), who were unaware of the clinical features and angiographic results, for the identification of the involved vascular territories. Three types of hemispheric BZI were herein considered: 'anterior' when the infarct occurred between MCA and ACA, 'posterior' between MCA and PCA (i.e. 'letzte Wiese' between the anterior and posterior circulation), and 'internal' between deep and superficial MCA perforators. Previous dementia was an exclusion criterion.

For all patients, language and swallowing disturbances were systematically assessed within the first 48 h. Including this initial screening, the patients had three standardized language evaluations performed by the same speech-language therapist (C-F R): (i) initially, i.e. within the first 48 h after admission (ii) at discharge

Table 1 General characteristics of our patients with aphasia because of BZ infarcts

Pt	Age/gender	Risk factors	Initial presentation	Initial NIHSS	BZI stroke location based on DW-MRI	Stroke mechanism
1	49/F	Hypertension, hypercholesterolemia	Aphasia, R-facial palsy	4	L-MCA/ACA and internal	Occlusion of the L-ICA
2	77/F	Hypertension, diabetes	Aphasia, R-hemiplegia and facial palsy	11	L-MCA/ACA, MCA/PCA and internal	> 70% L-ICA stenosis
3	73/M	Diabetes	Aphasia, R-hemianopia and facial palsy	5	L-MCA/PCA	50% L-ICA stenosis
4	64/M	Hypertension, smoking	Aphasia, R-hemianopia and facial palsy	6	Bilateral MCA/ACA and R-MCA/PCA	Sub-occlusive R-ICA stenosis
5	88/M	Hypertension, diabetes, smoking	Aphasia, R-hemiparesis and facial palsy	11	L-MCA /ACA L-MCA/PCA	Sub-occlusive L-ICA stenosis
6	74/M	Hypertension, diabetes, smoking, hypercholesterolemia	Aphasia, R-hemiparesis and facial palsy	6	L-MCA/ACA	50% L-ICA and L-MCA stenosis
7	60/M	Hypertension, hypercholesterolemia	Aphasia, R-facial palsy	3	L-MCA/ACA	Cardio-embolic
8	71/F	Hypertension	Aphasia, R-facial palsy	3	L-MCA/PCA	50% L-ICA and L-MCA stenosis

BZI, border-zone infarcts; Pt, patient number; F, female; M, male; L, left; R, right; MCA, ACA and PCA, respectively middle, anterior cerebral and posterior cerebral artery; ICA, internal carotid artery.

from stroke unit, and (iii) at long term, i.e. between 6 and 18 months after stroke. The first two language evaluations consisted in five oral subtests: three for examination of verbal production (naming pictures, word and sentence repetition, and automatic language) and two in order to evaluate the comprehension level (auditory comprehension and comprehension of simple, semi-complex, and complex orders). Between these two evaluations, patients had standard language rehabilitation. Between 6 and 18 months after stroke, the patient had a comprehensive language evaluation using the Boston Diagnostic Aphasia Evaluation (BDAE) scale (evaluating oral comprehension, oral agility, repetition, naming, oral reading, reading comprehension and writing, with 28 subtests) [14].

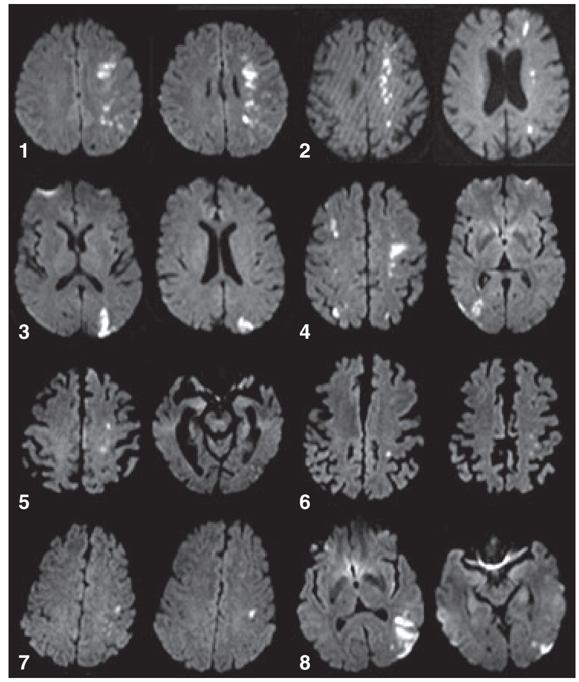

Figure 1 Cerebral diffusion-weighted MRI of the border-zone infarctions (BZI) associated with aphasia. Left *BZI* observed in patient 1 (MCA/ACA and internal); patient 2 (MCA/ACA, MCA/PCA and internal); patient 3 (MCA/PCA); patient 4 (bilateral MCA/ACA and right MCA/PCA); patient 5 (MCA/ACA and MCA/PCA); patient 6 (MCA/ACA); patient 7 (MCA/ACA) and patient 8 (MCA/PCA BZ infarction). MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery.

Results

Amongst 26 individuals with hemispheric BZI, eight patients satisfied our inclusion and exclusion criteria. The 18 others patients were excluded because (i) the BZI affected the non-dominant hemisphere (right BZI in right-handed patient: $n = 11$), (ii) the BZI was left but in ambidextrous ($n = 1$) or in left-handed patient ($n = 1$), (iii) because the patient was not French native speaker ($n = 4$) or (iv) because of associated acute encephalopathy (by alcohol abuse; $n = 1$). Their baseline characteristics are shown in Table 1. Initial cerebral MRIs are shown in Fig. 1.

Within 48 h after admission, all patients presented with a transcortical mixed aphasia, i.e. altered comprehension and naming difficulties including paraphasias, while repetition was preserved. Detailed results of language examination are shown in Table 2. None presented swallowing dysfunction.

During first days, aphasia rapidly evolved. At discharge from stroke unit, between day 3 and 15, three patients had totally recovered (patients 3, 4, and 5). In remaining patients, aphasia changed from transcortical mixed (TMxA) toward transcortical motor (TMoA) or sensory (TSeA) depending on stroke location (respectively, in anterior and posterior BZI). Indeed, three patients, all with anterior BZI, had transcortical motor aphasia (paraphasia, reduced speech with short sentences, associated with preserved comprehension and repetition) (patients 1, 6, and 7), whereas two had transcortical sensory aphasia (altered lexical and syntactic comprehension, associated with preserved naming and repetition) (patient 2 with both posterior and anterior BZI and patient 8 with an isolated posterior BZI).

Long-term language evaluation was performed between 6 and 18 months in seven patients (patient 6 was lost to follow-up). Amongst these seven patients, none kept residual aphasia. To note, despite no aphasia, they had features of mild executive/attention dysfunctions: low verbal fluency, attention deficit (essentially highlighted by the BDAE's subtest named 'logic and reasoning'). and/or alteration of working memory (verbal span) in 5/7, and/or hemianopsia [disclosed in picture description ($n = 2/7$)].

Discussion

Our study indicates evidence that aphasia associated with hemispheric BZI is initially of transcortical mixed type (TMxA) and later changes to TMoA or TSeA. This is in contrast with previous reports in which most BZI patients had transcortical sensory aphasia (TSeA) or transcortical motor aphasia (TMoA) [8,9]. This discrepancy might be because of the fact that our patients were all evaluated in the first 48 h. In previous series, the delay of language examination was not reported, and it may be that initial TMxA may have been overlooked because of a later evaluation. There are only two

Table 2 Initial, short-, and long-term language examinations

		Verbal production				Oral comprehension				
			Repetition				Orders			
Time at examination	Patient and timing	Naming	Word	Sentence	Automatic language	Auditive comprehension	Simple	Semi-complex	Complex	Type of aphasia
Initial stage D0-D3	Pt 1 D1	–	+	–	–	+	+	+	–	TMxA
	Pt 2 D3	–	+	–	+	–	–	–	–	TMxA
	Pt 3 D1	–	+	–	+	–	+	–	–	TMxA
	Pt 4 D1	–	+	+	+	+	+	+	–	TMxA
	Pt 5 D1	–	+	+	+	–	+	–	–	TMxA
	Pt 6 D0	–	+	–	+	–	–	–	–	TMxA
	Pt 7 D1	–	+	–	+	+	–	+	–	TMxA
	Pt 8 D1	–	+	+	+	–	–	–	–	TMxA
Subacute stage D3-D15	Pt 1 D6	–	+	–	+	+	+	+	+	TMoA
	Pt 2 D15	+	+	+	+	+	–	+	+	TSeA
	Pt 3 D3	+	+	+	+	+	+	+	+	No
	Pt 4 D3	+	+	+	+	+	+	+	+	No
	Pt 5 D4	+	+	+	+	+	+	+	+	No
	Pt 6 D1	–	+	+	+	+	+	+	+	TMoA
	Pt 7 D4	–	+	+	+	+	+	+	+	TMoA
	Pt 8 D3	+	+	+	+	–	+	+	+	TSeA
Tardive stage M6-M18	Pt 1 M18	+	+	+	+	+	+	+	+	No
	Pt 2 M18	+	+	+	+	+	+	+	+	No
	Pt 3 M16	+	+	+	+	+	+	+	+	No
	Pt 4 M13	+	+	+	+	+	+	+	+	No
	Pt 5 M17	+	+	+	+	+	+	+	+	No
	Pt 6									
	Pt 7 M7	+	+	+	+	+	+	+	+	No
	Pt 8 M6	+	+	+	+	+	+	+	+	No

Pt no, patient number; D, day after stroke; M, month; TMxA, Transcortical Mixed Aphasia; TMoA, Transcortical Motor Aphasia; TSeA, Transcortical Sensory Aphasia; No, No aphasia. Patient 6: No long-term evaluation (lost to follow-up).

reports on a total of four patients with TMxA associated with left hemispheric BZI [10,11]. Interestingly, preservation of the repetition is a common feature of all types of transcortical aphasia and could thus be a good clinical clue to suspect a left BZI even before MR imaging. Normal repetition could reflect the integrity of the arcuate fasciculus, the pre motor cortex and the temporal lobe, as lesions of these structures are usually associated with a repetition disorder as observed in conduction, Broca or Wernicke aphasia [15,16]. These findings appear useful in practice to suspect BZI because hemodynamic factors are often implicated in these infarctions and may justify specific urgent management such as surgery in tight internal carotid stenosis [with carotid endarteriectomy performed in 11 of our 26 patients with BZI (42%; data not shown)]. Inversely, to demonstrate that transcortical aphasia is predictive of BZI infarct, further studies are needed that will compare aphasic stroke patient with and without preserved repetition with respect to stroke location.

While all our patients with left BZI presented initially with a transcortical mixed aphasia, the subsequent pattern of aphasia depends on stroke location (TMoA in anterior BZI, and TSeA in posterior BZI, respectively). These short-term modifications of the aphasic pattern may be because of a transient initial hypoperfusion of apparently preserved territories (penumbra) and/or to an early reorganization of the neuronal networks [12,17,18]. Indeed, TMxA, called by Geschwind 'syndrome of isolation (of the speech area)' [19] because the perisylvian speech areas appear to be disconnected from the dominant hemisphere, can evolve toward TMoA or TSeA by re-connecting the supplementary motor area to Broca's area in one hand and parietal to occipital areas on the other hand [11]. Finally, we cannot exclude that long-term presence of hemodynamic compromise in our patients with carotid stenosis might also have induced some degree of cerebral reorganization prior to the stroke that may have favoured rapid recovery following stroke. While anatomical basis of transcortical aphasia remains unclear, its specific initial pattern in BZ infarcts which rapidly improved with good long-term prognosis underlines the need for additional complementary explorations. In such patients, functional MR imaging, including perfusion study and fiber tracking, with parallel language testing at acute phase and during language recovery could be informative [20]. Several explanations for impaired language and evolution in patients with BZI can be proposed including (i) loss of function, (ii) focal and transitory hypoperfusion (prolonged penumbra surrounding ischaemia), (iii) disruption of the language network owing to the infarction, resulting in a dysfunction in remote areas in terms of diaschisis and (iv) preserved repetition in BZI related to language reorganization involving the contralateral language area [21]. Knowing that all these hypothesis should be studied in functional MR imaging, further studies are needed in order to demonstrate activation, or up- or down-regulation of the left or the right homologue language network regions [20].

Our data, although based on a small number of patients, indicate that the long-term outcome of aphasia associated with BZI is excellent. All patients made a full language recovery within the 18 months following stroke. This aphasic pattern we described in patients with BZI, i.e. initial TMxA followed in a few days by TMoA or TSeA, with excellent long-term recovery, needs to be confirmed in larger series to evaluate its specificity, its usefulness in clinical practice as well as for speech therapy.

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The authors declare no financial or other conflict of interests.

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Initial presentation and course of aphasia due to watershed cerebral infarct. **C. Flamand-Rouviere,** C. Cauquil-Michon, R. Souillard-Scemama, C. Denier, D. Adams. (Communication affichée ; European Neurological Society ; Milan 2009)

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Présentation initiale et évolution des aphasies liées à un infarctus jonctionnel. **C. Flamand-Rouviere,** C. Cauquil-Michon, R. Souillard-Scemama, C. Denier, D. Adams. (Communication affichée ; Société Française de NeuroVasculaire; Paris 2008)

Evaluation précoce de l'aphasie en phase aiguë des AVC

L'incidence de l'aphasie après un accident vasculaire cérébral (AVC) diffère en fonction des étiologies, mais est globalement retrouvée dans 15 à 55% des cas (7,8,9,10). Sa fréquence est probablement plus élevée à la phase très précoce, c'est à dire dans les premiers jours qui suivent l'AVC. Les facteurs favorisants l'existence de troubles du langage lors d'AVC sont l'antécédent d'AVC, l'âge, le sexe féminin, et l'origine cardio-embolique (en particulier la fibrillation atriale) (11).

L'évolution des troubles phasiques peut être rapide : dans les 10 jours suivant l'AVC, on considère que 46% des aphasies auront notablement régressé et 21% auront spontanément disparu. Toutefois, les troubles du langage persistent chez environ la moitié des patients aphasiques 18 mois après l'AVC (10,13,14). Cela constitue une altération majeure de la qualité de vie, à l'origine de syndromes dépressifs fréquents. La persistance d'une aphasie s'associe à une moins bonne participation à toute forme de rééducation (kinésithérapie, ergothérapie...) par difficulté de communication, à un retrait social, une moindre probabilité de reprendre une vie professionnelle (12,16,17). Si il est convenu que l'aphasie résultant d'une hémorragie aura un meilleur pronostic que l'aphasie après une ischémie, il est difficile de prédire des évolutions au cas par cas. Actuellement, seul le score initial de sévérité de l'AVC (au NIHSS) semble prédictif : l'amélioration serait proportionnelle au déficit initial avec, comme pour la récupération motrice, une amélioration évaluable à 70 % environ du déficit initial à 3mois. (7,10).

Dans le cadre d'un AVC ischémique, le traitement le plus efficace, si il est administré dans les 4h30 suivant l'apparition des premiers signes, est le traitement par thrombolyse intra veineuse. Il comporte toutefois des risques de transformation hémorragique, il faut donc évaluer au plus juste les bénéfices qu'il apporterait, compte tenu de ce risque. Effectuer le bilan des lésions et de leur retentissement est primordial : cela permet d'envisager au mieux et au plus vite la prise en charge thérapeutique active médicamenteuse comme la rééducation. Pour cela, les neurologues disposent d'échelles validées et utilisées dans le monde entier. Le NIHSS (18) est une échelle globale qui donne un score avec un seuil en dessous duquel la balance bénéfice/risque n'est pas en faveur de l'utilisation du traitement. Ainsi, lors de l'arrivée en urgence d'un patient potentiellement candidat à une thrombolyse (« alerte thrombolyse »), le langage, comme les autres fonctions motrices et cognitives, doit être évalué de façon précise et reproductible, afin de mesurer au mieux la gravité de l'AVC. De même, détecter rapidement l'aphasie permet la mise en place d'une prise en charge précoce, et donc plus efficace en conjuguant la thérapie orthophonique intensive à la réorganisation neuronale post AVC de manière optimale. Dans le score du NIHSS, le langage est sous représenté, et son évaluation consiste en quelques questions sommaires, l'altération reposant alors sur l'impression clinique du médecin. Il est donc fréquent qu'un patient présentant un trouble du langage isolé ou associé à un trouble moteur léger ne bénéficie pas de la thrombolyse, le score à l'échelle NIHSS étant un critère d'inclusion ou d'exclusion : le score du NIHSS serait trop faible, le handicap trop léger, pour prendre le risque d' une transformation hémorragique.

Jusqu'à récemment, les tests validés pour évaluer les troubles du langage de façon fiable, qualitative et quantitative, étaient soit longs et fastidieux et donc inutilisables en phase aiguë des AVC, soit au contraire rapides, mais trop grossiers pour être pertinents et reproductibles. Les tests de langage de référence, administrés par les orthophonistes, tels le Boston Diagnosis Aphasia

Examination (BDAE), la Western Battery for Aphasia ou le Montréal Toulouse 86 sont robustes et complets, mais inadaptés en phase aiguë des AVC (19,20,21). En effet, le temps de passation de ces échelles de langage est de 30 minutes à deux heures de sorte qu'elles ne peuvent pas être proposées en phase aiguë. En effet, l'alerte thrombolyse est une situation d'urgence. , Il faut également prendre en compte la fatigabilité et d'éventuels troubles de la vigilance du patient lors de cette phase aiguë. De plus, les modifications rapides et les fluctuations du langage dans ce contexte rendent difficile l'évaluation qui risque, en fonction de l'outil utilisé, d'être biaisée par l'existence de troubles moteurs, praxiques, neuro-visuels, exécutifs ou de l'attention associée.
Les échelles plus générales conçues pour la phase aiguë de l'AVC, telles que le National Institute of Health Stroke Score (NIHSS), comprennent des items langage, mais ne sont pas assez précises pour appréhender efficacement l'aphasie qualitativement et quantitativement de façon reproductible d'un médecin à l'autre.

S'il existe des échelles d'évaluation de l'aphasie destinées à la phase aiguë, peu sont traduites en français ni même validées, et elles comportent souvent des items qui ne sont pas adaptés à cette situation (items de langage écrit, non-utilisables chez des patients avec hémiplégie ou chez les patients illettrés, utilisation de matériel visuel complexe qui biaisent les résultats des patients présentant une héminégligence ou une hémianopsie, temps d'administration trop long) (22).

Pourtant, le diagnostic précis et précoce des troubles du langage est nécessaire pour affiner la connaissance du déficit du patient dés son arrivée, pour distinguer l'aphasie d'autres atteintes cognitives ou fonctionnelles, et pour pouvoir mettre en place rapidement une rééducation adaptée. Il peut également permettre d'identifier plus précisément des phénotypes précoces spécifiques comme nous avons pu le montrer dans le cas particulier des aphasies liées aux infarctus jonctionnels (23).

Dans le cadre des AVC, chaque minute compte, et correspond à la destruction de 2 millions de neurones et de 14 milliards de synapses (24). Il manquait donc un outil fiable, rapide d'administration et validé pour évaluer l'aphasie dans ce contexte.

Fiche de recherche :
Rôle : **investigateur principal.** Conceptualisation, analyse, Rédaction du protocole pour obtention de l'accord du comité d'éthique de Bicêtre, administration du protocole, rédaction et soumission de l'article.
Equipe de recherche : Dr C. Denier (INSERM U788), Dr E. Roze (INSERM U952, CNRS UMR 7224 UPMC Paris 6), Pr B. Falissard (INSERM U669)
Nombre de patients : 450
Type de recherche : élaboration et validation d'échelle.
Site : CHU Bicêtre Service de neurologie adulte et USINV

Méthodes

Elaboration et conceptualisation de l'outil :

Il était indispensable que l'échelle soit :

- rapide à administrer, et donc comporter peu d'items. Les épreuves écrites ont été éliminées, car elles allongeaient le temps d'évaluation, n'étaient pas administrables aux patients hémiplégiques ou non lettrés, et n'avaient pas un intérêt essentiel (les troubles isolés du langage écrit sont extrêmement rares)
- fiable : les items devaient être les plus pertinents possibles et être choisis en fonction de leurs fréquences lexicales et visuelles dans la langue française, ainsi qu'en fonction de leurs structures phonétiques.
- composée uniquement d'items essentiels au diagnostic : dénomination, répétition, série automatique pour la partie « expression », désignation, exécution d'ordres pour la partie « compréhension ».
- reproductible quelque soit l'examinateur
- exempte d'effet re-test en cas de passation pré et post thrombolyse grâce à l'élaboration de deux versions strictement équivalentes

Description de l'outil :

LAST se compose :

- D'une épreuve de dénomination d'images, choisies pour leur fréquence sémantique et visuelle ainsi que pour leur niveau de difficulté phonémique;
- D'une épreuve de répétition (un mot et une phrase concrète) ;
- D'une série automatique (le comptage, peu soumis aux connaissances académiques) ;
- D'une épreuve de désignation d'images (quatre images parmi quatre pièges : sémantique, visuel, phonétique proche, phonétique lointain) choisies elles aussi pour leur fréquence visuelle et sémantique ;
- D'une épreuve d'exécution de trois ordres (simple, semi- complexe et complexe).

Au total, le patient obtient un score sur 15. LAST doit pouvoir être administré aussi bien par un orthophoniste que par un non-spécialiste du langage (médecin, étudiant, infirmière, autre rééducateur), avec la même fiabilité. Cette évaluation doit pouvoir se faire au lit du malade, dès son arrivée, et participer au processus décisionnel thérapeutique (thrombolyse). Enfin, nous avons créé deux versions de cette échelle, LAST-A et LAST-B, qui devront être strictement équivalentes afin de pouvoir être administrées alternativement à différentes étapes de l'évolution du patient pour permettre une évaluation quantitative de l'évolution.

Validation de l'outil :

Nous avons d'abord présenté l'échelle à 50 témoins, tous âges, sexes et niveau socio-culturels confondus, afin de s'assurer qu'aucun item ne posait de difficulté ou ne présentait d'ambiguïté.
Puis nous avons testé :

- la validation interne de LAST et sa validité inter-examinateur sur 300 patients consécutifs en phase aigüe d'un AVC.
- sa validité externe et l'équivalence des versions A et B sur 150 patients présentant une aphasie chronique (afin d'administrer également le « gold standard » BDAE pour comparer les deux résultats, ce qui n'est pas envisageable sur des patients en phase aigüe en raison de leur fatigabilité et de la longueur de passation de ces tests).
- le temps de passation moyen sur 50 patients consécutifs en phase aigüe d'un AVC.

Résultats et répercussions :

La validation interne a montré qu'aucun item ne montrait d'effet plafond ou plancher, ni de redondance. La validation externe, par rapport au BDAE, la batterie d'évaluation du langage classiquement utilisée en phase de chronicité, nous a permis d'établir un cut-off à 14 : un score inférieur à 15 doit alors justifier la passation d'autres évaluations plus poussées, tant sur le plan arthrique que phasique, et permettre ainsi la prise en charge en rééducation précoce si cela s'avère nécessaire. Les deux versions LAST-A et LAST-B sont strictement équivalentes. Le temps de passation de LAST est en moyenne de deux minutes. La validité inter-juge montre que les résultats sont fiables quelque soit l'examinateur.

LAST (Language Screening test) est le premier test screening publié et validé en français. Il permet de dépister un trouble phasique en phase aigue d'un AVC, une amélioration de la connaissance du tableau clinique du patient, une meilleure analyse du déficit, afin que la présence d'une aphasie soit prise en compte dans le processus décisionnel de thrombolyse. Depuis sa publication, LAST est de plus en plus présente dans les Unités de soins intensifs neurovasculaires, et son utilisation s'étend à d'autres services (voir chapitre 3). Au-delà de son intérêt pour la pratique clinique quotidienne, Les caractéristiques de LAST et la qualité de sa validation en font potentiellement un outil de choix pour évaluer l'aphasie dans le cadre de futures études interventionnelles à la phase aigue de l'accident vasculaire.

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Validation of a New Language Screening Tool for Patients With Acute Stroke : The Language Screening Test (LAST)

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Validation of a New Language Screening Tool for Patients With Acute Stroke

The Language Screening Test (LAST)

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Background and Purpose**—**Standard aphasia scales such as the Boston Diagnosis Aphasia Evaluation are inappropriate for use in acute stroke. Likewise, global stroke scales do not reliably detect aphasia, and existing brief aphasia screening scales suitable for patients with stroke have several limitations. The objective of this study was to generate and validate a bedside language screening tool, the Language Screening Test, suitable for use in the emergency setting.

Methods**—**The Language Screening Test comprises 5 subtests and a total of 15 items. To avoid retest bias, we created 2 parallel versions of the scale. We report the equivalence of the 2 versions, their internal and external validity, and their interrater reliability. We validated the scale by administering it to 300 consecutive patients within 24 hours after admission to our stroke unit and to 104 stabilized patients with and without aphasia using the Boston Diagnosis Aphasia Evaluation as a reference.

Results**—**The 2 versions of the Language Screening Test were equivalent with an intraclass correlation coefficient of 0.96. Internal validity was good; none of the items showed a floor or ceiling effect with no redundancy and good internal consistency (Cronbach α 0.88). External validation against the Boston Diagnosis Aphasia Evaluation showed a sensitivity of 0.98 and a specificity of 1. Interrater agreement was near perfect (intraclass correlation coefficient, 0.998). The median time to complete the Language Screening Test was approximately 2 minutes. Importantly, the Language Screening Test does not need to be administered by a speech and language therapist.

Conclusions**—**This comprehensively validated language rating scale is simple and rapid, making it a useful tool for bedside evaluation of patients with acute stroke in routine clinical practice. **(*Stroke*. 2011;42:1224-1229.)**

Key Words: aphasia ■ diagnostic tool ■ rating scale ■ stroke ■ validation study

Poststroke aphasia is a major source of disability, potentially leading to impaired communication, reduced social activity, depression, and a lower probability of resuming work.[1–4] Despite some controversy, early detection of aphasia after stroke may improve rehabilitation by taking advantage of the synergy between intensive speech therapy and early neural reorganization.[5–7] Tools capable of detecting aphasia and evaluating its severity during the acute phase of stroke might help to improve early rehabilitation and to predict outcome.[8] Standard aphasia rating scales such as the Western Aphasia Battery, the Boston Diagnostic Aphasia Evaluation (BDAE), and the Boston Naming Test are not appropriate for use during the acute phase of stroke.[7,9–11] In particular, these scales take too long to complete and must be administered by speech and language therapists.[9–11] Global stroke rating scales such as the National Institutes of Health Stroke Scale and the Scandinavian Stroke Scale include language items and have been developed for use in acute settings,[12–17] but they do not reliably detect aphasia.[8] Several attempts have been made to develop and validate brief aphasia screening scales suitable for patients with acute stroke,[5,18–25] but all have inherent structural limitations, including[7] (1) inclusion of written language subtests, the results of which are influenced by hemiplegia and illiteracy[5,19–23,25]; (2) use of complex visual material inappropriate for patients with stroke with neurovisual deficits[19,20]; (3) inclusion of subtests the results of which are markedly influenced by attention/executive dysfunction[19,20]; (4) excessively lengthy administra-

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Expression index *(maximum score = 8 points)*
- **naming:** 5 pictures *(from 0 to 5 points)*
- **repetition:** one concrete four-syllable word and one eight-words sentence containing 11 syllables and three consonantal groups *(from 0 to 2 points)*
- **automatic speech:** *counting from 1 to 10 (0 to 1 point)*

Receptive index *(maximum score = 7 points)*
- **recognition:** 4 pictures among 4 traps *(from 0 to 4 points)*
- **verbal instructions:** simple, semi-complex and complex order *(from 0 to 3 points)*

Total LAST score: maximum score = 15 points

Figure 1. Design of the Language Screening Test (LAST). LAST comprises 5 subtests and a total of 15 items. Each item is scored 1 (perfect answer) or 0 (imperfect answer, including arthric errors, and failure to answer) after an interval of 5 seconds. The maximum score is 15.

tion[22]; (5) difficulties with administration or scoring[5,18,23,25]; and (6) IQ dependency.[21] Some of these scales also have poor sensitivity for the detection of language disorders and a paucity of information on their validity and reliability.[5,20]

We therefore developed a brief language screening scale, named the Language Screening Test (LAST), for the assessment of patients with acute stroke. LAST incorporates the following features: (1) no written material; (2) no complex visual material; (3) no evaluation of verbal executive function; and (4) suitability for bedside administration by persons who are not speech and language therapists. We report the validity, reliability, sensitivity, and specificity of LAST.

Patients and Methods

Scale Construction

LAST was developed as a formalized quantitative scale for screening language functions, including comprehension and expression. The initial, qualitative design phase focused on item generation and construction. We chose to exclude verbal fluency subtests, the results of which are strongly influenced by changes in attention/executive function, and also written language subtests that are unsuitable for hemiplegic and illiterate patients. We generated several preliminary versions of the scale, which were evaluated internally and then refined because of the following weaknesses: (1) too lengthy to administer (too many items); (2) in the naming task, inadequate use of real daily objects such as watches and pens, instead of images, which are less ambiguous (for example, the pen of 1 examiner is different from the pen of another one); and (3) in the picture recognition task, inadequate use of color pictures, which may provide semantic clues. We selected the items by consensus and eliminated any ambiguities by administering the scale to 50 healthy volunteers (data not shown).

The final version of LAST consists of 5 subtests and a total of 15 items (Figure 1). The patient has 5 seconds to answer each question, and the answer is scored as either 1 (perfect answer) or 0 (imperfect answer, including arthric errors, and failure to answer). The maximum score is therefore 15. There are 2 subscores, namely an expression index (naming, repetition, and automatic speech; maximum score 8 points) and a receptive index (picture recognition and verbal instructions; maximum score 7 points).

The test is administered on a simple sheet held in portrait orientation. The front side corresponds to the expression index with 5 pictures to be named facing the patient and the instructions facing the examiner. The other side corresponds to the receptive index with 8 pictures (4 to be indicated with a finger and 4 trap pictures) facing the patient and the instructions facing the examiner (see Supplemental Data; http://stroke.ahajournals.org).

Each subtest is composed as follows (Figure 1):

(1) "Naming" subtest: naming of 5 black-and-white pictures specially drawn for the test. The pictures were selected for their everyday familiarity (subjective verbal frequency) and for the image evoking value of the noun.[26] Standard synonyms and abbreviations are accepted (alligator for crocodile, TV for television, etc). The maximum score is 5 points.
(2) "Repetition" subtest: repetition of 1 concrete 4-syllable noun and 1 8-word sentence containing 11 syllables and 3 consonantal groups. One self-correction is accepted. The maximum score is 2 points, 1 for the isolated word and 1 for the sentence.
(3) "Automatic speech" subtest: the patient counts from 1 to 10. No mistakes or omissions are accepted. The score is 1 or 0.
(4) "Picture recognition" subtest: recognition of 4 black-and-white pictures drawn specially for the test and selected for their high image-evoking value and sorted by their subjective verbal frequency. This subtest includes 2 phonologic traps (close and distant), 1 semantic and 1 visual. The maximum score is 4.
(5) "Verbal instructions" subtest: execution of 3 verbal orders—simple, semicomplex, and complex—involving the use of part of the body or simple objects in the room. The patient is asked to precisely execute the verbal order. The maximum score is 3.

Having developed a version of the scale that we considered suitable for validation (LAST-a), we then generated a second, parallel version (LAST-b). Each item on the 2 scales was different (except for the automatic speech item, see subsequently) but strictly matched to obtain 2 equivalent versions of the scale. For example, the pictures (naming subtest and recognition subtest) used in the 2 versions were each matched for their visual and verbal frequency, and the words and sentences used for the repetition subtest were matched for their consonantal content. Several series can be used to assess automatic speech, but counting is the most universally acquired (days of the week and the alphabet, for example, are more influenced by sociocultural status). Counting to 10 was thus used in both versions (see Supplemental Data).

Patients and Instruments

To validate the scale, we included both "acute" and "chronic" patients. We first prospectively enrolled consecutive "acute" patients, that is, admitted with suspected acute stroke to our stroke unit during a 7-month period. They were tested within 24 hours after their admission. During the same period, we enrolled stabilized patients (hospitalized or ambulatory) seen in our neurology department, but not in the stroke unit, who were able to complete the entire BDAE comprehensive language evaluation. These "chronic" patients were considered aphasic or nonaphasic on the basis of their BDAE results. The BDAE is a standard scale widely used for comprehensive evaluation of aphasia. Its 28 subtests evaluate oral comprehension, oral agility, repetition, naming, oral reading, reading comprehension, and writing and take between 1.5 and 2 hours to administer.[10] Both "acute" and "chronic" patients were excluded if they had any of the following characteristics: (1) history of dementia or of severe psychiatric disorders; (2) deafness or blindness; (3) nonnative French language; and (4) altered consciousness. The study was approved by the ethics committee of Pitié-Salpêtrière Hospital, Paris. Demographic data were collected for all the patients and the National Institutes of Health Stroke Scale score was recorded for the "acute" patients. A schematic representation of the study design is shown in Figure 2.

Validation of LAST

LAST was validated on the basis of (1) the equivalence of the 2 versions of the instrument; (2) the internal validity of the 2 versions of the instrument (item analysis, reliability, and factor structure); (3) external validity (comparison with the BDAE scale); and (4) interrater reliability.

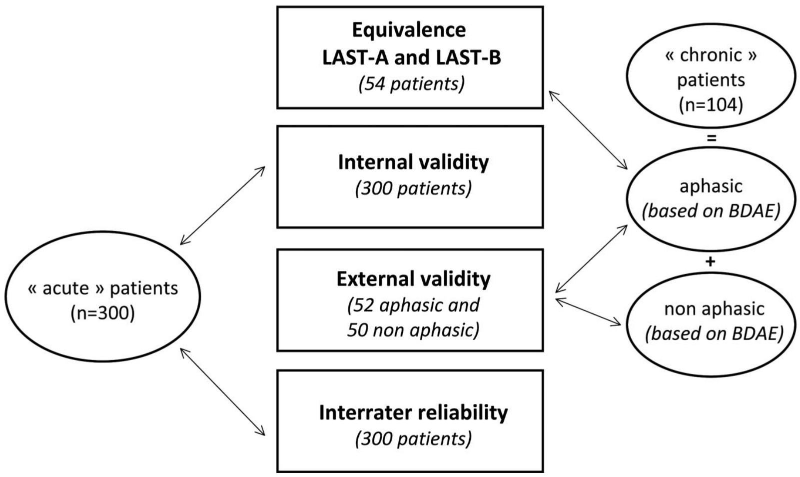

Figure 2. Schematic representation of the Language Screening Test (LAST) validation process. Please note that the time taken to administer LAST was estimated using 50 new consecutive patients who are not represented on this figure.

To test the equivalence of the 2 versions of LAST, the "chronic" aphasic patients were asked to complete LAST-a followed by LAST-b with a 1-minute rest period.

To assess the internal validity of the scale, consecutive "acute" patients completed either LAST-a or LAST-b within 24 hours after admission. The 2 versions were used in alternation for each new patient (only 1 version per patient).

To assess external validity, aphasic and nonaphasic "chronic" patients were asked to complete the BDAE language evaluation followed by either LAST-a or LAST-b on the same day and administered by 2 different and blinded examiners.

Interrater reliability was assessed in the "acute" patients. Four examiners pairs were used, consisting of a speech and language therapist with another speech and language therapist, a student, a nurse, or a neurologist. All the examiners received a 5-minute explanation on how to administer the test. Blinded assessment was ensured as follows. Two examiners were present at the bedside. The first examiner administered LAST to the patient (result used for internal validity), reading aloud 1 by 1 the different subtest, at the same time as the second examiner, who could hear the first examiner but could not see the results he or she recorded, simultaneously scored the same version.

The median time for scale completion was calculated for 50 new consecutive "acute" patients.

Statistical Analysis

The concordance of the 2 versions of LAST was assessed by calculating the intraclass correlation coefficient (ICC) from the 2 total scores (equivalent to a quadratic weighted κ).

Internal validity was assessed in 3 steps. First, we closely inspected the score distribution for each item to detect a floor or ceiling effect, and the Pearson correlation matrix was used to detect item redundancy. Second, the number of underlying dimensions was determined by parallel analysis, which consists of representing a traditional screeplot with simulations.[27,28] Third, we calculated Cronbach α coefficient, a measure of reliability based on internal correlation of the items on the scale.

To evaluate external validity, sensitivity and specificity were assessed with respect to the BDAE. We represented the correlations between the LAST and BDAE subtests on a sphere (Figure 3)[29] and with the receiver operating characteristic curve (Figure 4).

The ICC was used to appreciate interrater reliability.

R 2.11.1 software and the "psy" library were used for all analyses.[30]

Results

Sample Description

Three hundred forty consecutive unselected "acute" patients were admitted to our stroke unit for suspected acute stroke during a 7-month period. Thirty-six patients were excluded (nonnative French speakers [n=24], history of dementia or severe psychiatric disorders [n=6], deafness or blindness [n=3], altered consciousness [n=3]) and 4 could not be evaluated for logistic reasons. The remaining 300 "acute" patients were included in the internal validity and interrater reliability assessments (159 men and 141 women; mean age 62.6 years [±14.9]; mean National Institutes of Health Stroke Scale score 3.5 [±5.1]; Figure 2).

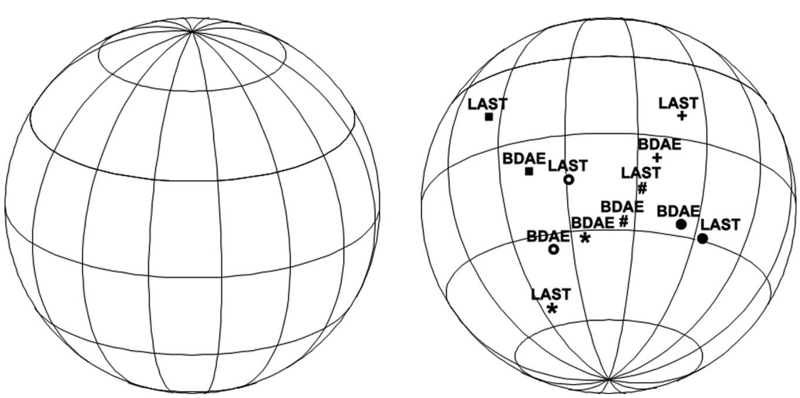

Figure 3. Spherical representation of the correlation matrix of the Language Screening Test (LAST) subtests and corresponding Boston Diagnostic Aphasia Evaluation (BDAE) items. # Naming (LAST: 5 items/5 points; BDAE: 35 items/105 points); O word repetition (LAST: 1 item/1 point; BDAE: 20 items/10 points); ■ sentence repetition (LAST: 1 item/1 point; BDAE: 16 items/16 points); * automatic speech (LAST: 1 series/1 point; BDAE: 3 series/9 points); ● picture recognition (LAST: 4 items/4 points; BDAE: 36 items/72 points); + verbal instructions (LAST: 3 orders/3 points; BDAE: 5 orders/15 points).

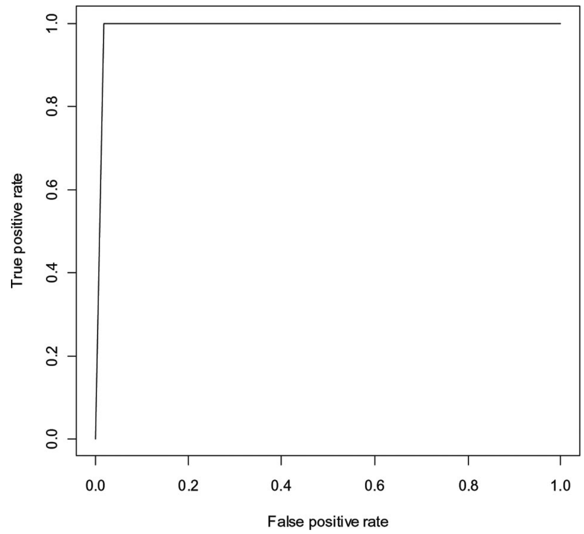

Figure 4. Receiver operating characteristic (ROC) curve showings the sensibility (true-positive rate) and 1-specificity (false-positive rate) of Language Screening Test (LAST) in comparison with the Boston Diagnostic Aphasia Evaluation (BDAE) used for external validation. The optimal cutoff for the LAST score corresponds to the angle of the curve in the upper left-hand corner of the diagram. At that point (LAST <15), specificity=1 and sensibility=0.98.

The sample of 104 "chronic" patient consisted of 55 men and 49 women with a mean age of 61.6 years (±17.9). Based on the BDAE results, 54 of these "chronic" patients (30 men and 24 women, mean age 66.4 years [±11.0]) had aphasia and were used to study the equivalence of the 2 versions of LAST. To assess external validity, we used the results for the 50 "chronic" patients without aphasia (25 men and 25 women; mean age 56.4 years [±16.2]) and 52 "chronic" patients with aphasia (27 men and 25 women; mean age 67.4 years [±14.8]; mean LAST score 9.9 [±3.9]). Two patients refused the BDAE (Figure 2).

Time Taken to Administer LAST

The median time required to complete LAST was 124 seconds (interquartile range, 80).

Equivalence of LAST-a and LAST-b

The comparison of LAST-a and LAST-b in the sample of 54 "chronic" aphasic patients showed that the 2 versions were strictly equivalent with an ICC of 0.96. Exclusion of the automatic speech item, which is identical in the 2 versions, did not significantly modify the ICC (0.954). None of the patients diagnosed as "aphasic" in 1 of the versions was "nonaphasic" in the other version. The same level of agreement was observed for each item of the scale.

Internal Validity

Because LAST-a and LAST-b were equivalent, data obtained with the 2 versions were pooled for analysis. Similar results were obtained with LAST-a, LAST-b, and the 2 versions combined. Item-by-item analysis of the whole sample of 300 "acute" patients showed no floor or ceiling effect. There was no redundancy between items as shown by Pearson correlation coefficients <0.8. Parallel analysis revealed a 1-dimensional structure. The internal consistency of the 15 items was good with a Cronbach α of 0.88.

External Validity

Taking the BDAE as the gold standard, LAST had a sensitivity of 0.98 for aphasia and a specificity of 1 with a cutoff of <15 in the sample of 102 "chronic" patients. Thus, only 1 patient identified as "aphasic" with the BDAE obtained a score of 15 out of 15 in LAST, whereas all patients with a LAST score of <15 were diagnosed as "aphasic" with the BDAE. A spherical representation of the correlation matrix of the LAST and BDAE subtests is shown in Figure 3 (the closer the points, the stronger the correlation). The receiver operating characteristic curve in Figure 4 shows the nearness of the results of the 2 tests by the tradeoff between sensitivity and specificity with a 2-dimensional measure of classification performance: the closer the receiver operating characteristic curve is to the upper left-hand corner, the higher the overall accuracy of the test.[31]

Interrater Reliability

Interrater reliability for the 300 "acute" patients was near perfect (ICC, 0.998). The results obtained by the examiner pairs consisting of 2 speech and language therapists (26%) were not different from those of the pairs combining a speech and language therapist with a nurse (32%), student (34%), or a neurologist (8%). The ICC was near perfect regardless of the nature of the second examiner.

Discussion

We have developed and validated a brief language screening scale (LAST) for patients with acute stroke. LAST standardizes and formalizes quantitative clinical language examination in the emergency setting. The scale has good internal validity, correlates well with the gold standard BDAE scale, shows very high interrater reliability, and is quick to complete. We developed 2 versions of the scale to avoid the retest bias and found that the 2 versions were equivalent. Importantly, LAST does not need to be administered by a speech and language therapist. With a cutoff score of <15 from a maximal score of 15, LAST showed excellent sensitivity and specificity for language disorders, thus identifying patients warranting personalized language evaluation with a speech and language therapist. Although the benefit of language therapy during the acute phase of stroke is controversial, this screening tool may help to begin early language rehabilitation, which may optimize long-term rehabilitation.[5–7] One strength and originality of LAST is the possibility of using the 2 versions successively to test the same patient, thereby avoiding the retest effect.

LAST detected a language deficit (score <15, the cutoff based on external validation) in 55% of the 300 patients admitted urgently to our stroke unit during the study period, whereas aphasia is reported in only 17% to 38% of patients in other acute stroke series.[32] Explanations for this difference may include (1) a higher sensitivity of LAST for aphasia in this setting; (2) early testing in our study (within 24 hours after admission), thus identifying patients who would go on to recover rapidly[33]; and (3) identification of false-positive (nonaphasic) patients such as (a) patients with dysarthria (8% to 30% of patients in large stroke series have isolated dysarthria)[34,35]; and (b) patients with visual field impairment, eye movement disorders, or initiative/executive dysfunctions (for example, the maximal response time of 5 seconds could penalize patients with initiative disorders). Lastly, although we excluded patients with a history of dementia or severe psychiatric disorders, deafness or blindness, altered consciousness, or a non-French native language, such patients could undermine the reliability of LAST results in a real-life setting. Although we included consecutive patients, we acknowledge that they were rather young with fairly mild strokes when compared with the literature's stroke series. Possible reasons for these particular characteristics are: (1) the oldest patients with stroke are preferentially admitted to geriatric acute care units; and (2) patients with more severe stroke are occasionally admitted to nonspecialized intensive care units. This may have resulted in a slight recruitment bias. Concerning the potential limitations of our validation procedure, we had no alternative to testing external validity in "chronic" patients, because (1) there is no universally recognized gold standard scale for evaluating language disorders in the emergency setting; and (2) gold standard aphasia rating scales such as BDAE take too long to administer in acute stroke. In contrast, internal validity, interrater reliability, and the time required for scale completion were determined in "acute" patients. Finally, LAST was primarily designed to evaluate language impairment, but it is now well recognized that the impact on daily life activities of such impairments extends beyond these actual impairment,[36] and tools have recently been developed to specifically address this issue.[37,38] It would be interesting to test LAST against such quality-of-life scales.

The impact of very early intervention (within days after stroke) on language recovery is difficult to screen, and LAST may prove useful for this purpose. However, to further establish its use, future studies are warranted comparing LAST and language items of the National Institutes of Health Stroke Scale against BDAE or another gold standard. A recent Cochrane review showed a benefit of speech and language therapy in patients with stroke but failed to establish the best way of delivering such therapy or the best time to initiate speech and language therapy.[39] This review was based on 30 randomized trials of various interventions designed to improve language in patients with stroke, but none of the studies focused on very early interventions, starting within 15 days after stroke. As a result, the use of the usual prevalent tools such as BDAE was warranted. By contrast, a recent randomized controlled trial of very early intervention (Day 2) used a short adjusted home-made version of the Norsk Grunntest for Afasi. This scale was not validated, included written items, and took 15 minutes to complete, which limited its use to selected patients.[40] The paucity of the literature on very early interventions and the use of nonvalidated scales underlines the need for new validated tools such as the LAST scale.

In conclusion, we propose a new validated language screening tool for patients with acute stroke, which can be administered at the bedside in approximately 2 minutes. This French-language scale should be easy to adapt to English and other languages. It may represent a useful complement to global stroke rating scales such as the National Institutes of Health Stroke Scale for initial evaluation of patients with stroke.

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Disclosures

None.

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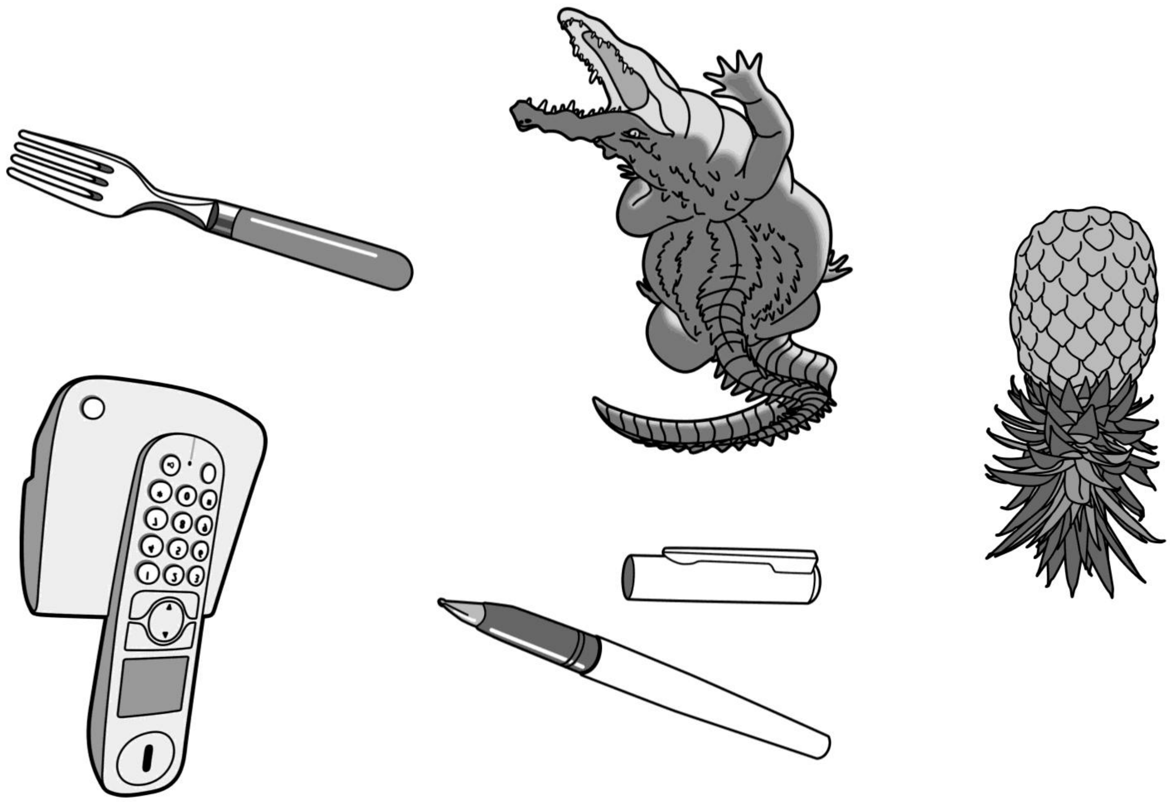
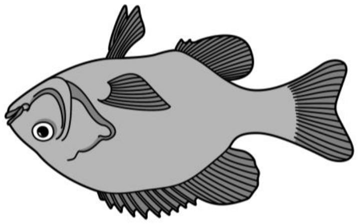


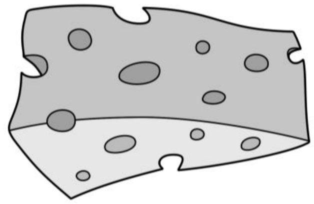
Language Screening Test
LAST-a

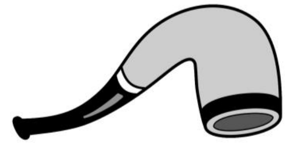
Nom du patient

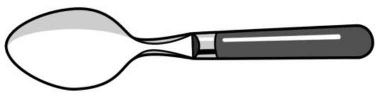
Date : ___/____/_____

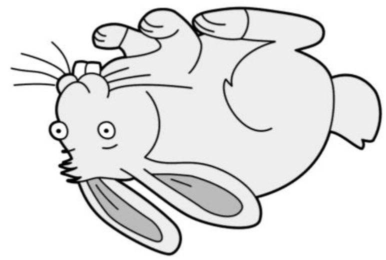
Expression orale		SCORE	
Dénomination	Téléphone	/1	
	Ananas	/1	
	Stylo	/1	
	Crocodile	/1	
	Fourchette	/1	
	Score dénomination		***/5***
Répétition	Mathématiques	/1	
	Le facteur apporte une lettre chez ma voisine	/1	
	Score répétition		***/2***
Série automatique	Compter de 1 à 10	/1	
	Score série automatique		***/1***
Score total expression orale			**/8**

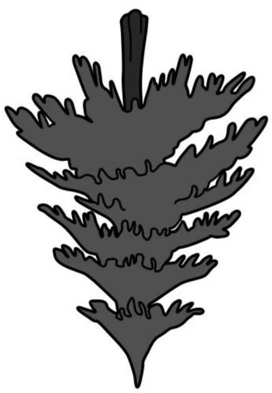


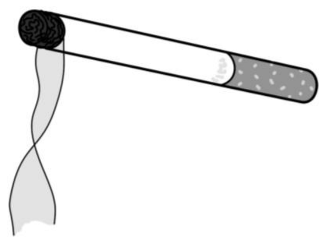




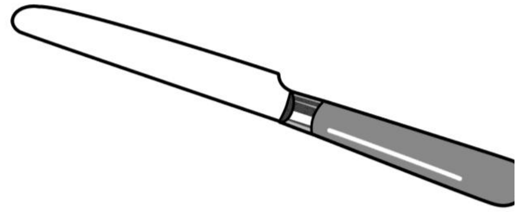


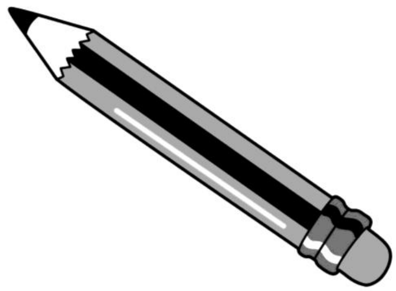


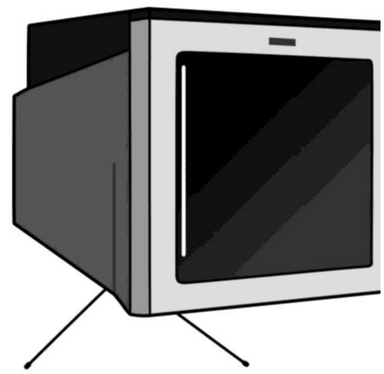




Compréhension orale		Score	
Désignation	Lapin	/1	
	Cuillère	/1	
	Cigarette	/1	
	Œil	/1	
	Score désignation		/4
Exécution d'ordres	« Montrez le plafond »	/1	
	« Ne prenez pas le verre mais le stylo »	/1	
	« Mettez une main sur la tête puis un doigt sur le nez »	/1	
	Score exécution d'ordres		**/2**
Score total compréhension orale			**/7**
SCORE LAST TOTAL		**/15**	





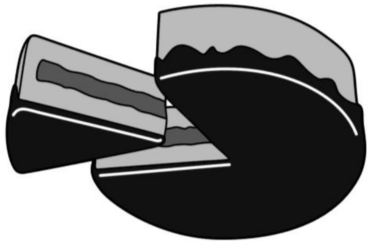
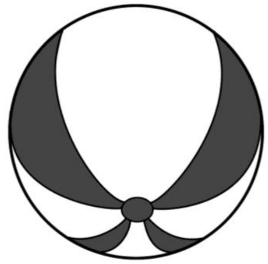
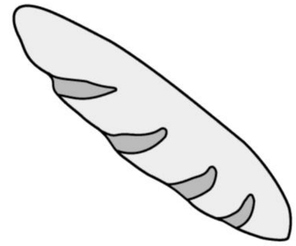
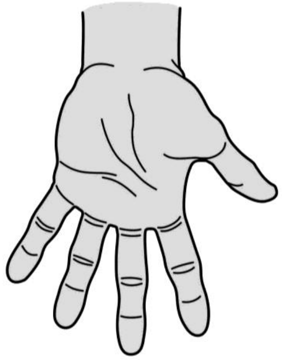
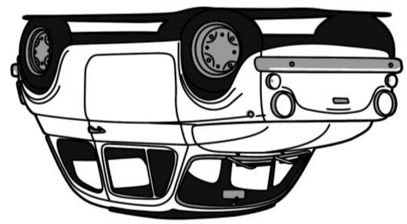
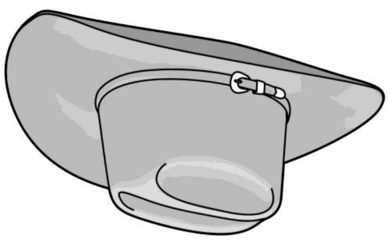
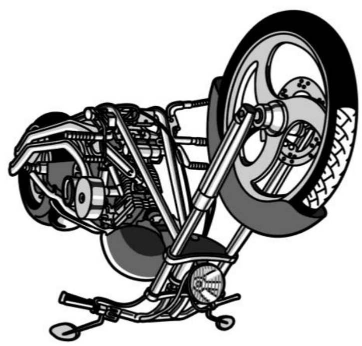
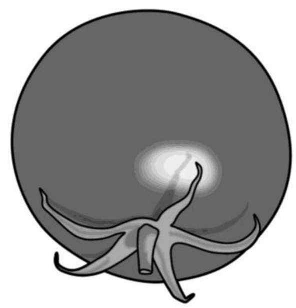


Language Screening Test
LAST-b

Nom du patient

Date : ___/____/_____

Expression orale		SCORE	
Dénomination	Crayon	/1	
	Télévision	/1	
	Girafe	/1	
	Couteau	/1	
	Papillon	/1	
	Score dénomination		***/5***
Répétition	Littérature	/1	
	Les vacanciers voudraient des glaces à la fraise	/1	
	Score répétition		***/2***
Série automatique	Compter de 1 à 10	/1	
	Score série automatique		***/1***
Score total expression orale			***/8***

Compréhension orale		Score	
Désignation	Chapeau	/1	
	Main	/1	
	Voiture	/1	
	Tomate	/1	
	Score désignation		/4
Exécution d'ordres	« Montrez le sol »	/1	
	« Ne prenez pas la feuille mais la clef »	/1	
	« Touchez une de vos oreilles avec un doigt, puis votre front avec deux doigts »	/1	
	Score exécution d'ordres		**/2**
Score total compréhension orale			**/7**
SCORE LAST TOTAL		**/15**	

Exploitation, valorisation et diffusion des résultats :

Etude publiée dans la revue **Stroke (impact factor : 6.0)**

Présentations dans des congrès nationaux et internationaux :

Une échelle de détection rapide de l'aphasie en phase aiguë des accidents vasculaires cérébraux : Language Screening Test (LAST). **C. Flamand-Roze,** C. Denier.(Présentation orale ; Réunion paramédicale de la Société Française Neurovasculaire ; Journées de Neurologie de Langue Française; Nice 2012)

Elaboration et validation d'un outil rapide de dépistage de l'aphasie en phase aiguë des accidents vasculaires cérébraux : le Language Screening Test (LAST) **C. Flamand-Roze,** B. Falissard, E. Roze, C. Denier(Communication affichée ; Société française de NeuroVasculaire; Paris 2011)

Validation of a new language screening tool for acute stroke patients: the Language Screening Test (LAST). **C. Flamand-Roze,** B. Falissard, E. Roze, C. Denier. (Communication affichée ; European Federation of Neurological Society ; Budapest2011)

Validation of a new language screening tool for acute stroke patients: the Language Screening Test (LAST). **C. Flamand-Roze,** B. Falissard, E. Roze, C. Denier. (Communication affichée ; American Academy of Neurology ; Honolulu 2011)

Présentation de LAST dans les services de neurologie vasculaire de l'Assistance Publique Hôpitaux de Paris et de France (régions).

Dépôt d'une enveloppe Soleau.

Evaluation précoce des aphasies en phase aiguë des AVC - Extensions

Depuis la création de l'outil, celui-ci est utilisé dans les différentes Unités de soins intensifs neurovasculaires de France : dans les services de neurologie de l'AP-HP, Lyon, Bretagne, Meaux, Cachan, Garches, Châtellerault, Bar Le Duc, Arras, Nancy, Niort, CH Charentes, Arriège, La Roche sur Yon, Aubagne, CHR Creil, Metz, Béziers, Castres, Lille, Vichy..., mais également à l'étranger : Italie, Espagne, Royaume Unis, Hongrie, République Tchèque, Turquie, Belgique, USA, Australie, Canada (Québec, Toronto) Chine, Indonésie, Tunisie, Maroc... Son utilisation est enseignée dans les écoles d'orthophonie, auprès des étudiants en médecine et également dans les Instituts de Formation en Soins Infirmiers. L'utilisation de LAST en tant qu'outil validé va permettre de réaliser différentes études, en disposant d'un outil fiable. Ainsi, plusieurs extensions sont en cours.

Exemples d'utilisation en pratique clinique :

LAST étant un outil rapide, fiable et pratique, les équipes médicales et paramédicales l'utilisent au cours de l'hospitalisation, afin d'évaluer les progrès des patients, et de pouvoir apporter des informations concrètes aux familles. Cet outil permet également une harmonisation entre les services : chaque service testait le langage de manières différente, sans consensus. Le score LAST est maintenant intégré dans les comptes rendus médicaux des patients et est compris par chaque équipe qui recevra le patient par la suite. Ceci n'a pas encore était étudié de façon systématique.

A l'hôpital de Bicêtre, 25 patients présentant une aphasie isolée (sans hémiplégie associée), ont bénéficié du traitement par thrombolyse malgré un score NIHSS (score permettant de quantifier le déficit du patient lors d'un AVC) trop faible (en prenant en compte le rapport bénéfice / risque hémorragique). En d'autres termes, LAST a permis une évaluation de la sévérité globale du tableau clinique accordant un poids plus juste à une aphasie initiale sévère, compte tenu de son impact prévisible sur la qualité de vie ultérieure. Sur cette base, l'intégration du score LAST au processus décisionnel a donc permis de proposer le traitement à davantage de patients. Ces 20 patients sont régulièrement suivis en consultation externe, et tous ont retrouvé leur niveau de langage antérieur à l'AVC. Une publication sur ce sujet est en cours (dernier auteur). Les résultats de cette étude ont été présentés lors du congrès JNLF (Journées de Neurologie de langue française) en 2013 (présentation a été primée) :

Thrombolyse et aphasies isolées : au-delà du score NIHSS**. C. Flamand-Roze,** M. Sarov, S.Depuydt, E.Roze, C.Denier (communication affichée primée. JNLF, Montpellier 2013)

Extension à d'autres conditions :

Un projet de validation de LAST pour la détection des troubles phasiques dans les maladies neurodégénratives. Cela permettrait d'évaluer rapidement le niveau de langage d'un patient qui présente une plainte, afin de faire la part des choses entre une difficulté mnésique et une aphasie primaire progressive, par exemple. LAST pourrait alors être utilisé systématiquement dans les consultations mémoire, ou chez les généralistes qui reçoivent les patients en première intention, avant d'adresser ou non les patients vers un orthophoniste ou un neuropsychologue pour affiner les évaluations avec des tests spécifiques. Ce projet est une collaboration avec le Dr Emmanuel Roze, le Dr Stéphane Epelbaum, le Dr Marc Teichman et le Pr Bruno Dubois à la Pitié Salpétrière.

Extension à d'autres langues :

LAST est un test de langage, il est donc étroitement lié à la langue même dans laquelle il est administré. Les items qui composent LAST ont été choisis en fonction de leurs fréquences dans la langue ou de leur structure. Une simple traduction ne remplirait pas tous les critères qui ont permis à LAST de si bons résultats de validation. Différentes services ont donc décidé d'adapter LAST dans leur langue. Le processus d'adaptation à l'anglais a fait l'objet de présentations lors de congrès internationaux, et d'une publication. D'autres adaptations sont en cours, en chinois, allemand, québécois et portugais brésilien.

Fiche de recherche :
Rôle : **Collaboratrice.**
Equipe de recherche : Dr C. Denier (INSERM U788), Dr E. Roze (INSERM U952, CNRS UMR7224 UPMC Paris 6), Pr B. Falissard (INSERM U669)
Pour l'adaptation en anglais (Canada, USA, Grande Bretagne et Australie) : H. Flowers, A. McGovern, K. Baumwol, C. Langdon, G. Harris, S. Tyson, L. Burton, K. Brooks
Pour l'adaptation en chinois : Dr Z. Liang
Pour l'adaptation en allemand : M. Koenig-Bruhin
Pour l'adaptation en portugais brésilien : R. de Lima Ramos
Pour l'adaptation en québécois : L. Monetta, J. Bourgeois-Marcotte.
Nombre de patients : 150 pour la validation en anglais ; 50 pour la validation en québécois ; A déterminer pour les autres pays concernés.
Type de recherche : Adaptation d'échelle.
Sites : CHU Bicêtre ; University of Toronto, Pitié Salpétrière, Toronto Western Hospital, Greater Manchester and Chesshire cardiac and stroke network, Sir Charles Gardner Hospital Australia, Tongji Medical College, Huazhong University of Science & Technology Wuhan, Hubei, China, Centre hospitalier de Bienne Suisse, Science college of clinics hospital, Sao Paulo Brazil, Université de Laval, Québec, Canada.

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English adaptation, international harmonisation, and normative validation of the Language Screening Test (LAST)

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Background: The Language Screening Test (LAST) is a unique bedside tool, designed to rapidly and reliably evaluate aphasia during the acute and chronic phases of stroke. Two equivalent reliable and validated versions of the LAST exist in French.
Aims: Our objective was to conduct a linguistic adaptation for English (LASTen) through a process of translation, international harmonisation, and normalisation in multiple English-speaking countries.
Methods & Procedures: There were four progressive stages in the adaptation of the LASTen including a series of sequential evaluations to identify problematic items, with selection of alternatives by consensus and in collaboration with the original LAST developers. First, three Canadian translators independently adapted the 29 items of the original LAST into English, resolving discrepancies by consensus to produce adaptation I. Evaluations of adaptation I involved ratings of translation difficulty and multidisciplinary expert panel review to produce adaptation II. Evaluations of adaptation II included ratings of translation quality by three different translators followed by healthy native speaker testing in Canada to produce adaptation III. Evaluations of adaptation III included expert review in Australia, Canada, England, and the USA for cultural acceptability and naturalness, followed by healthy native speaker testing in all the four countries to produce adaptation IV. Adaptation IV constituted a linguistically valid LASTen for four English dialects. We documented consensus decisions to modify or retain problematic items. We evaluated group differences using the Kruskal–Wallis test for continuous variables and chi-squared analyses for frequency variables with statistical significance of alpha $\leq .05$.
Outcomes & Results: During the translation and the evaluations, we reconsidered 22 of the 29 items, revising 20 to produce adaptation IV of the LASTen. Normative testing in the four English-speaking countries involved 109 participants (mean age 60 years, *SD* ±16.1). Fifty-five percent were women, and 32% lacked postsecondary education. Fourteen participants made errors across nine items. There were no significant differences in errors for age, sex, or country. However, participants with postsecondary education made fewer errors than those without ($p = .04$).
Conclusions: We achieved a linguistically compatible adaptation of the French LAST for English, confirming naturalness and cultural appropriateness in healthy native speakers of four English dialects. Our systematic multistep approach delineates

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rigorous methods for the adaptation of aphasia tools. Our normative validation of the LASTen in healthy native speakers of English provides the impetus for its validation in stroke patients within the four English-speaking countries.

Keywords: stroke; screening; aphasia; international harmonisation; linguistic validation

Post-stroke aphasia is a major source of disability, incurring increased use of rehabilitation services (Dickey et al., 2010) and cost of care (Ellis, Simpson, Bonilha, Mauldin, & Simpson, 2012). It also has negative economic repercussions, including decreased return to work (Dalemans, De Witte, Wade, & Van den Heuvel, 2008; Graham, Pereira, & Teasell, 2011). Aphasia may be difficult to systematically identify in the acute stage through usual care (Flowers, Silver, Fang, Rochon, & Martino, 2013). Early diagnosis of aphasia often relies on informal and cursory bedside screening or evaluation, usually conducted by front-line health care professionals, such as nurses and/or emergency room doctors. Without rapid and validated screening tools, accurate identification of aphasia may be lacking, and acute aphasia assessments may ensue in only a subset of patients at risk.

Given the potential inadequate capture of aphasia, management by speech–language pathologists (SLP) may be sorely compromised, especially early after stroke onset. Implementing acute screening and assessment protocols will ensure best practice in the management of aphasia. Accurate and timely identification of aphasia is paramount to commencing treatment early after stroke, which has been shown to be feasible (Laska, Kahan, Hellblom, Murray, & Von Arbin, 2008) and efficacious (Godecke, Hird, Lalor, Rai, & Phillips, 2012). Early and efficacious treatment in patients with aphasia will improve outcomes such as severity of aphasia and participation in communication (Godecke et al., 2012). Finding the best means to facilitate recovery from aphasia comprises a top research priority following stroke (Pollock, St George, Fenton, & Firkins, 2012). Accordingly, investigators should align their research agendas and clinicians their day-to-day clinical goals with clinical management concerns, to promote patient-oriented care (Liberati, 2011). The development of a rapid and valid aphasia screening tool is a crucial first step to address the needs of stroke survivors with aphasia, who desire more service by SLPs (Worrall et al., 2011). Routine screening for aphasia can guide the trajectory of care early after stroke onset, by facilitating the rapid identification of patients requiring early and/or sustained management by SLPs.

Acute aphasia screening tools

Screening is important for timely capture of potential risk of an impairment. Routine implementation of a screening protocol permits rapid assessment for accurate diagnosis and appropriate management of an impairment. There is a lack of reliable and validated aphasia screening tools in English that are appropriate for the early detection and repeat evaluation of post-stroke aphasia. A recent review identified six post-stroke aphasia screening tools that had supporting psychometric evaluation in the acute stage (Salter, Jutai, Foley, Hellings, & Teasell, 2006). They included the Frenchay Aphasia Screening Test (FAST) (Al-Khawaja, Wade, & Collin, 1996; Enderby & Crow, 1996; Enderby, Wood, Wade, & Langton Hewer, 1987), the Mississippi Screening Test (MAST) (Nakase-Thompson et al., 2005), the Acute Aphasia Screening Protocol (AASP) (Crary, Haak, & Malinsky, 1989), the Aphasia Screening Test (ASE) (Reitan, 1985), the Screeling (Doesborgh et al., 2003), and the Ulleval Aphasia Screening (UAS) (Thommessen, Thoresen, Bautz-Holter, & Laake, 1999). In addition, two recently developed and validated tools designed for acute stage aphasia screening include the Language Screening

Test (LAST) (Flamand-Roze et al., 2011) and the Aphasia Rapid Test (ART) (Azuar et al., 2013).

Many of the existing screening tools lack validation against standardised batteries (Azuar et al., 2013; Enderby & Crow, 1996; Enderby et al., 1987; Nakase-Thompson et al., 2005), involve a lengthy administration (Doesborgh et al., 2003; Reitan, 1985), include items that rely upon executive functions (Azuar et al., 2013; Crary et al., 1989; Doesborgh et al., 2003; Enderby et al., 1987; Nakase-Thompson et al., 2005; Reitan, 1985), or are not available in English (Azuar et al., 2013; Doesborgh et al., 2003; Flamand-Roze et al., 2011; Thommessen et al., 1999). The recent development of the LAST is a response to the need for well-designed rapid aphasia screening tools (Flamand-Roze et al., 2011). The LAST is a brief screen (median completion time: 124 s) that includes two versions to avoid retest effects (LAST-a and LAST-b) (Flamand-Roze et al., 2011). Compared to the other language screening tools, the LAST has better psychometric validation, limits task demands to those required in language processing, and is more practical for an acute stroke setting (Flamand-Roze et al., 2011).

Psychometric properties

The original LAST validation involved 102 consecutive stroke patients with screening for the presence versus absence of aphasia compared to the Boston Diagnostic Aphasia Examination (BDAE) (Goodglass & Kaplan, 1983), demonstrating a sensitivity of 0.98 and specificity of 1.0 (Flamand-Roze et al., 2011). Two other screening tools have also used concurrent validation to a gold standard but failed to systematically evaluate all patients (Doesborgh et al., 2003; Thommessen et al., 1999). The UAS validation involved 38 stroke patients and compared screening to assessments by SLPs (with partial administration of an aphasia battery), demonstrating a sensitivity of 0.75 and specificity of 0.90 (Thommessen et al., 1999). The Screeling validation compared screening of 63 stroke patients against a diagnosis of aphasia based on two of three positive evaluations (assessment by a neurologist, a linguist, and/or the token test), demonstrating a sensitivity of 0.92 and specificity of 0.96 (Doesborgh et al., 2003).

Other aphasia screening validations involved comparing the performance of stroke patients to healthy controls (Enderby et al., 1987; Nakase-Thompson et al., 2005) and/or have correlated screening scores to standardised batteries in patients with aphasia (Azuar et al., 2013; Crary et al., 1989; Enderby & Crow, 1996; Enderby et al., 1987). The MAST validation compared 36 healthy speakers to 38 left hemisphere and 20 right hemisphere stroke patients, demonstrating significant differences in total means scores across the three groups (Nakase-Thompson et al., 2005). Initial validation of the FAST compared screening performance in 50 stroke patients to 123 healthy participants, with a consequent proposed pass cut-off of >23/30 (Enderby et al., 1987).

Comparisons to a standardised battery in patients with aphasia have allowed for recovery prediction (Azuar et al., 2013) or determination of correlations between screening and test battery scores (Enderby & Crow, 1996; Enderby et al., 1987). The ART validation compared the acute screening scores of 37 patients with aphasia to 3-month dichotomised BDAE severity scores, predicting good 3-month recovery with a sensitivity of 94.4% and a specificity of 78.9% (Azuar et al., 2013). Comparison of the FAST to the Functional Communication Profile (Sarno, 1969) in two studies of 14 (Enderby et al., 1987) and 25 stroke patients with aphasia demonstrated correlations of .87 (Enderby et al., 1987) and .73 (Enderby & Crow, 1996) for total scores, respectively. The latter study also demonstrated a correlation of .91 (Enderby & Crow, 1996) between the FAST and the shortened Minnesota Test for the Differential Diagnosis of Aphasia (Powell, Bailey, & Clark, 1980). The AASP comparison to the Western Aphasia Battery (Kertesz, 1982) in 48 patients with aphasia demonstrated a correlation of .93 for total scores (Crary et al., 1989). Although useful for aphasia management, such comparisons lack the potential to discriminate between the presence versus absence of aphasia.

The ASE lacks comparison to a standardised aphasia battery, but the original full test, the Halstead-Reitan Neuropsychological Battery, has undergone multiple validations (Reitan, 1985). One study explored screening-internal correlations among eight abilities tested in the ASE, with aggregate results for 81 patients with stroke, 86 with closed head injury, and 30 with brain tumour (Williams & Shane, 1986). Correlations among abilities revealed two factors, one relating to verbal language and the other to sensorimotor coordination, thereby permitting potential dissociation of language impairment from other impairments for screening purposes (Williams & Shane, 1986). Performance relative to a standardised aphasia battery in patients with and without aphasia is still necessary for the ART (Azuar et al., 2013), the ASE (Reitan, 1985), the MAST (Nakase-Thompson et al., 2005), the FAST (Enderby et al., 1987), and the AASP (Crary et al., 1989).

Task constructs

Although complete dissociation between language and executive functions may be difficult, LAST items contain processing demands that are specific to language. For example, verbal fluency tasks may confound language proficiency, as they require prior response tracking or intrusion blocking (Kemper & McDowd, 2008). Consequently, a verbal fluency task is absent in the LAST, (Flamand-Roze et al., 2011), whereas four other screenings (Azuar et al., 2013; Crary et al., 1989; Enderby et al., 1987; Nakase-Thompson et al., 2005) include semantic category fluency (Azuar et al., 2013; Crary et al., 1989; Enderby et al., 1987) or discourse fluency (Nakase-Thompson et al., 2005). Additionally, metalinguistic tasks are present in the Screeling, including grammaticality judgements, semantic judgements, and backwards reading of single words (Doesborgh et al., 2003). Similarly, the ASE includes tasks requiring arithmetic computations (Reitan, 1985). Of the eight existing screenings, only the LAST (Flamand-Roze et al., 2011) and the UAS (Thommessen et al., 1999) do not include tasks involving executive functions.

Practicality

Some of the existing screenings limit practicality due to length of administration, complexity of tasks or cultural reasons. The Screeling requires a 15 min time to completion (Doesborgh et al., 2003), while the FAST, the AASP, and the MAST may take up to 10 min (Crary et al., 1989; Enderby et al., 1987; Nakase-Thompson et al., 2005). Many of the existing screenings require reading and writing and may not be suitable for illiterate patients or for those with visual impairments (Doesborgh et al., 2003; Enderby et al., 1987; Nakase-Thompson et al., 2005; Reitan, 1985; Thommessen et al., 1999). Only three screenings do not require reading and writing, the AASP (Crary et al., 1989), a separately validated oral language subscale of the FAST (Enderby et al., 1987) and the LAST (Flamand-Roze et al., 2011). Other administrative limitations include multiple proposed variations for scoring the ASE (Russell, Neuringer, & Goldstein, 1970; Wheeler & Reitan, 1962) and the inclusion of material specific to a given country (Nakase-Thompson et al., 2005) or culture (Reitan, 1985).

Because of its excellent psychometric properties, its construct validity, and its practicality, the LAST meets recent criteria for developing routine screenings (Eusebi, 2013) and aphasia tests in any language (Ivanova & Hallowell, 2013). Since the LAST is only available in French (Flamand-Roze et al., 2011), its adaptation into other languages is necessary. Adapting a routine aphasia screening into another language requires careful consideration of its conceptual framework and of its inherent linguistic properties. The LAST subtests follow a clinical-neuroanatomical framework for aphasia. They relate to general language functions such as auditory comprehension, repetition, automatic speech, and naming (Ivanova & Hallowell, 2013). They are exclusive to oral language modalities, thereby accommodating patients with varying education levels and socio-economic backgrounds (Flamand-Roze et al., 2011). The validation of the LAST against the BDAE (Goodglass & Kaplan, 1983) confirmed the applicability of the LAST to patients with heterogeneous aphasia types and severity levels (Ivanova & Hallowell, 2013). Similarly, the sample involved patients with ischemic stroke and intracerebral haemorrhage in both acute and chronic phases (Flamand-Roze et al., 2011), appropriately addressing a broad capture of patients for routine screening (Eusebi, 2013). The design ensured a comprehensive capture of the linguistic properties of French, relating to four linguistic domains: phonology, semantics, morphology, and syntax (Ivanova & Hallowell, 2013). Adaptation of the LAST into English requires evaluation of the same linguistic properties to establish construct validity and linguistic comparability. We have implemented rigorous multi-step translation and evaluation methods to adapt the LAST into American, Australian, British,[1] and Canadian dialects of English.

Linguistic variation in English dialects

Linguistic differences in the four dialects occur most frequently across phonological and semantic domains, while morphological and/or syntactic differences are rarer. Phonological differences may result from systemic phonotactic constraints or from phonemic variation in a given lexical item (Kerswill, 2014). Phonotactic constraints may induce ellipsis of an entire syllable or phoneme. For example, “literature” has four syllables in North American English, but only three in Australian and British English. Similarly, the production of syllable-final post-vocalic /r/ involves two phonemes in words such as “far” in North American English (/ɑr/) versus one elongated vowel (/ɑ:/) in British and Australian English (Sundkvist, 2009).

Systemic context-driven changes result in multiple words exhibiting the same dialect-specific phonotactic constraints. For example, “Canadian raising” involves raising of the low central vowel in the diphthongs /aw/ and /ay/ to a mid central vowel, /^w/ and /^y/ prior to syllable-final voiceless consonants, as in the words “about” and “nice” (Sadlier-Brown, 2012). Similarly, in North American and Australian English, vocalic assimilation with fronting of /ɑ/ to /æ/ occurs prior to the alveolar nasal consonant /n/, as “dance” and “can’t” (Labov, Ash, & Bober, 2006). Lexical phonemic variation occurs in isolated words, such as the production of “route” as /ruwt/ in Canadian, Australian, and British English but as /rawt/ in American English.

There are numerous semantic differences across the four dialects. For example, North Americans use the word “candy” to denote a small sugary treat, the English “sweet”, and Australians “lolly”. Shoes used for sports are termed “sneakers” in American and Australian English, “running shoes” in Canadian English, and “trainers” in British English. Australians use many short forms for common words, such as “arvo” for “afternoon” and “ute” for “utility vehicle”.

Syntactic and/or morphological differences are rarer but may arise in discourse. For example, the interjection “eh”, placed at the end of a sentence or phrase, is common in Canadian English (Gold & Tremblay, 2006). “Eh” has multiple discourse functions, including questioning, exclaiming, or providing an opinion as in “Nice day, eh?” (Gold & Tremblay, 2006). Similarly, in Australian English, appending the conjunction “but” sentence finally is prevalent, as in “I like that bag. It’s too expensive but” (Mulder & Thompson, 2008). Dialectal differences that potentially affect phonemic representation of words, use of morphemes, or word order require great consideration in international harmonisation of a tool. Equivalent linguistic properties across dialects should be present in the tool and must also reflect the most natural expression of language for all dialects.

Purpose

The overarching goal of the current study was to report on the international harmonisation and normative validation of the English LAST across four dialects, as a precursor to its validation and routine use in stroke patients. Objectives included the primary adaptation from French into English followed by international harmonisation with normative testing to ensure naturalness for multiple English dialects. We adapted the LAST into English using a multistep process to maintain the linguistic properties and processing demands of all items according to sociolinguistic, lexical, morphosyntactic, and phonotactic constraints.

Methods

Materials

There are two versions of the LAST (LAST-a, LAST-b), each containing five subtests. Each version consists of two subscores, an expressive language index (naming, repetition, and automatic speech) and a receptive language index (picture identification and verbal commands) (Flamand-Roze et al., 2011). Three of the subtests are in the oral expression index and two in the receptive language index. The oral expression index has eight items, resulting in a possible total subscore of 8, while the comprehension index has seven items, resulting in a possible subscore of 7. The expressive index includes naming of five original black and white pictures, repetition of one word and one sentence, and production of an automatic series (Flamand-Roze et al., 2011). The automatic series task is identical in both versions (Flamand-Roze et al., 2011). The receptive index includes recognition of four original black and white pictures (among four foils, one semantic, one visual, and two phonemic) and comprehension of one simple, one semi-complex, and one complex (two-step) verbal command (Flamand-Roze et al., 2011). Each item is given a score of 1 if correct and 0 if incorrect or inappropriate (Flamand-Roze et al., 2011). There are 15 items in each version, yielding a total of 29 unique items, given the one identical item in both the versions (Flamand-Roze et al., 2011).

Adaptation procedures

We used previously documented procedures for the translation of psychological tests (American Educational Research Association [AERA], 1999; International Test Commission [ITC], 2010; Jeanrie & Bertrand, 1999) and patient-reported outcomes (Acquadro, Conway, Hareendran, & Aaronson, 2008; Bullinger et al., 1998). To appraise the translation, we incorporated and evaluated progressive adaptations (Figure 1). The process of reconsidering items facilitates necessary evaluation of equivalence to the source version (Jeanrie & Bertrand, 1999). Each progressive adaptation of the two LAST versions (LAST-a and LAST-b) underwent two evaluations for a total of six evaluations. The intention for the final stage and consequent fourth adaptation was to

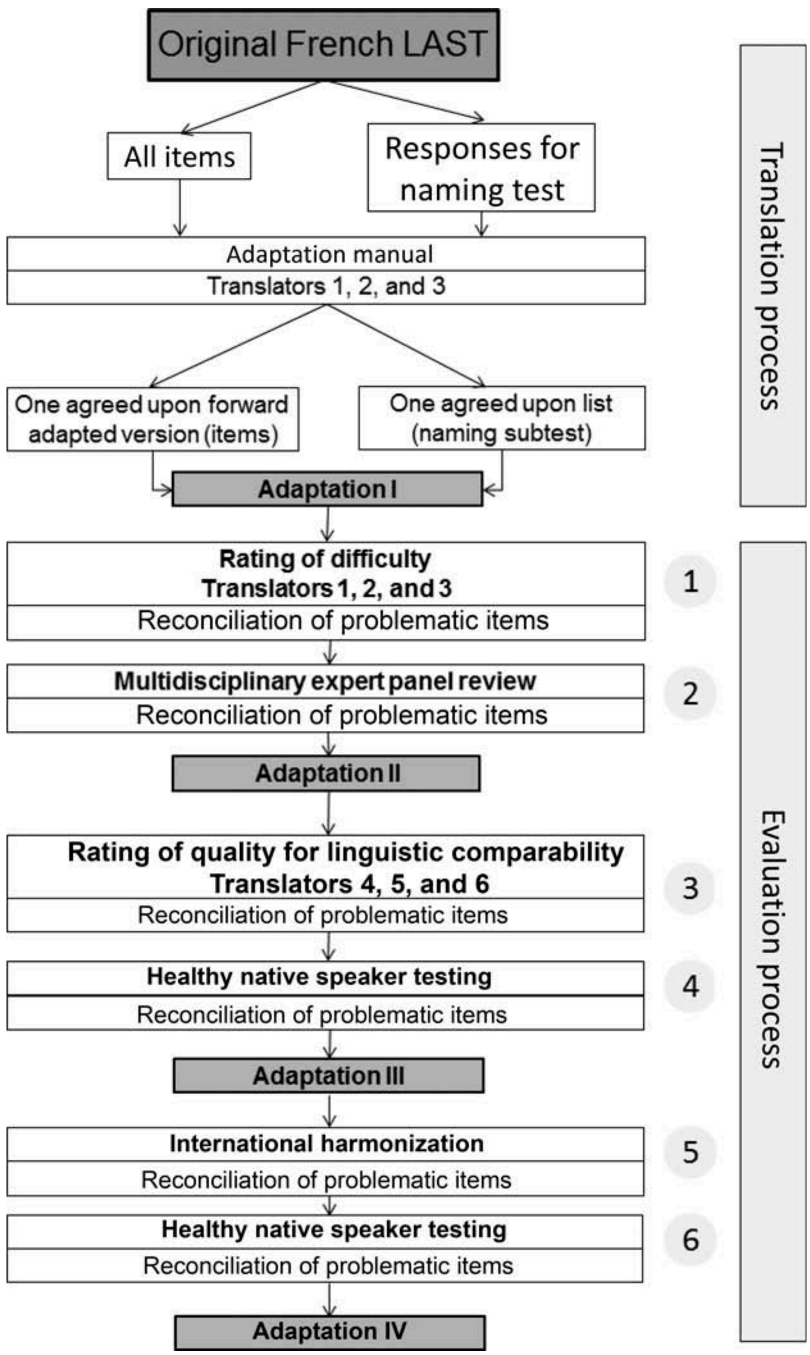

Figure 1. Adaptation procedures based on (Bullinger et al. (1998), AERA (1999), and Acquadro et al. (2008)).

produce a linguistically valid LASTen. Throughout the process, we reconciled problematic items after each evaluation by consensus and in consultation with the original LAST developers (Acquadro et al., 2008).

Translation

Three bilingual translators conducted independent translations of the 29 items of the LAST-a and LAST-b. All were native speakers of Canadian English and had lived in France for periods ranging between 5 and 19 months. According to recent recommendations for the translation of health questionnaires, only one translator had a background in health care (Acquadro et al., 2008). The three translators included an SLP, a language and literacy consultant for a regional board of education, and a digital marketing manager for a multinational bilingual corporation.

We developed an adaptation guide for the translators, delineating linguistic priorities in the four domains (phonology, morphology, semantics, and syntax) to retain the original linguistic criteria and to ensure comparable naturalness and language processing demands between the original and the English translation. Semantic comparability included the relative frequency of word or sentence level concepts between the two languages. Phonemic comparability included the relative frequency of phonemes according to the languages' phonemic repertoires and comparable complexity of syllabification and phonotactic constraints. Morphological comparability related to the inclusion of comparable morphological complexity and total number of morphemes. Finally, syntactic comparability related to equivalence of sentence level grammatical complexity. For the naming and picture identification subtests, we accorded highest priority to semantic and phonological comparability. For the automatic speech subtest, semantic comparability constituted the highest priority, and for the repetition and verbal command subtests, comparability in all four linguistic domains required careful consideration. The translators independently adapted all items into English, providing multiple translations per item as desired. They later collectively compared the three independent translations, resolving discrepancies by consensus to produce adaptation I of LASTen-a and LASTen-b.

Adaptation I evaluations

Adaptation I consisted of two evaluations. For the first evaluation, translators received verbal instructions and written explanations in the adaptation manual to help them derive difficulty ratings. Instructions required translators to independently rate each proposed translation using a whole number from 0 (not at all difficult) to 100 (extremely difficult) (Bullinger et al., 1998). Therefore, a rating of 0 denoted translations that easily captured equivalent linguistic information, while a rating of 100 denoted translations that were very inadequate in capturing comparable cultural and linguistic information. Previous literature in the translation of health tools used a threshold of mean difficulty ratings >25 across translators (Bullinger et al., 1998) to identify potentially problematic items. We used a more stringent criterion, reconsidering any items with a difficulty rating above 25 by a single translator to ensure adequate discussion and consideration of linguistic equivalence for all problematic items.

The second evaluation included a multidisciplinary panel of five experts in different disciplines: translation, linguistics, neurology, aphasia, and clinical epidemiology. They reviewed the English adaptation, proposing modifications of problematic items and resolving discrepancies by consensus. Modifications from adaptation I evaluations resulted in adaptation II of LASTen.

Adaptation II evaluations

Adaptation II consisted of two evaluations. For the first evaluation, we recruited three new translators to rate translation quality. All three were bilingual and native speakers of Canadian English. One had lived in France for 24 months, and the other two had completed secondary schooling in French and English. One was an SLP, and two were educators. We developed another adaptation guide with instructions and associated examples, to enable the three new translators to independently appraise the quality of the 29 items. Ratings included whole numbers from 0 (not at all perfect) to 100 (perfect) across four categories (n = 116 total ratings per translator): clarity (Bullinger et al., 1998), common language use (Bullinger et al., 1998), conceptual equivalence (Bullinger et al., 1998), and neurolinguistic equivalence. We derived the first three quality categories from previous work in the translation of questionnaires (Bullinger et al., 1998) and added the fourth category pertaining to the comparability of language processing demands in the English translation compared to the original.

Translators judged: (1) whether the verbal language and/or pictures were simple and understandable (i.e., unambiguous) for the category "clarity" (Bullinger et al., 1998); (2) whether the language was natural, avoiding technical and unnatural language for the category "common language use" (Bullinger et al., 1998); and (3) whether the concepts represented those in the original tool for the category "conceptual equivalence" (Bullinger et al., 1998). In addition, translators rated the category "neurolinguistic equivalence", by judging whether the language processing demands were comparable to those in the original tool. That is, any cross-linguistic discrepancies in demands in one or more of the four linguistic domains constituted evidence for poorer translation quality for a given item. Discrepancies could include concerns of either simpler or more complex phonological, morphological, semantic, or syntactic constructs in one language compared to the other. We reconsidered items rated below 75 by any translator for any quality category (Bullinger et al., 1998).

The second evaluation involved testing and interviewing a convenience sample of 10 healthy native speakers of Canadian English. We obtained ethical exemptions from the University of Toronto for native speaker testing in Canada. The participants had a mean age of 72.2 years (±12.7) and a median age of 75 years (range 40–88 years). Four were women, and seven had completed postsecondary education. We documented errors or problematic items during test administration, solicited additional acceptable terms for the naming subtest, and requested that participants name the picture identification foils to ensure clarity of depiction. Modifications based on these two evaluations resulted in adaptation III.

Adaptation III evaluations

Adaptation III consisted of two evaluations. For the first evaluation, experts from the four countries reviewed each item for linguistic acceptability according to the four linguistic domains: phonology, morphology, semantics, and syntax. Also, any proposed items or modifications had to meet the criterion of most natural spoken language for each dialect. A discrepancy in naturalness of language across dialects might relate to differences in language use, such as the exclusive use of "autumn" in British and Australian English, compared to the more predominant use of “fall” in North American English. Consequently, “autumn” would be a linguistically acceptable word for all four dialects, but not most natural for spoken North American English.

We required at least one consulting SLP from each country. In England, there were three experts, a researcher for the Stroke and Vascular Research Centre at University of Manchester, a knowledge translation partnership associate for the Greater Manchester and Cheshire Cardiac and Stroke Network, and an SLP. In Canada, experts included researchers in aphasiology and clinical epidemiology, a neurologist, and two SLPs undertaking doctoral studies. In the United States, the consulting expert was an American SLP undertaking doctoral studies. In Australia, experts included a researcher for Workforce, Education, and Reform in the Western Australia Department of Health and two senior SLPs at the Sir Charles Gairdner Hospital.

For the second evaluation, we conducted normative testing and interviews to ensure linguistic sensibility, using the same procedures as for adaptation II. We obtained ethical exemptions from the University of Toronto for native speaker testing in Canada and the United States, from the Sir Charles Gairdner Hospital for Australia, and from the Greater Manchester and Cheshire Cardiac and Stroke Network for England. In each country, we identified new convenience samples of ≥20 healthy native speakers through personal contacts or through recruitment from public places (e.g., airports). Experts were responsible for attempting to recruit participants with comparable gender and age demographics of stroke patients in their respective countries. Age and gender stroke statistics are comparable across the four countries with approximate mean age of 70 years and more frequent strokes occurring in women (Canadian Stroke Network, 2011; Hankey et al., 2000; Lee, Shafe, & Cowie, 2011; Petrea et al., 2009). The consulting experts in each country and/or other SLPs conducted the testing and later retested any modified items in samples of ≥10 of the same or new participants to establish adaptation IV of LASTen.

The normative sample consisted of 109 healthy older native English speakers of English in the four countries with a mean age of 60 years (±16.1), ranging from 23 to 93. Sixty (55%) were women. Nine reported potential difficulty with language testing due to hearing loss (n = 5), inadequate visual aids (n = 2), or previous but resolved nonstroke neurological compromise (n = 2). There were two rounds of testing to accommodate retesting of modified items. The initial normative testing involved 84 of the 109 participants, while 46 participants (25 new participants and 21 repeat participants) constituted those recruited to confirm revised items. The first group had a mean age of 59.9 years (±16.4) and 46 were women (55%). Eighty (95%) had completed secondary education and 54 (64%) postsecondary education. The second group of 46 participants had a mean age of 58.9 (±16.1) years and 25 (54%) were women.

Documentation

We documented the number of problematic items and resulting modifications following each of the six evaluations. We compiled the reasons for modifications within four categories: administrative, cultural, linguistic, or language processing (see examples in Figure 2). Administrative reasons included modifications to eliminate ambiguity in instructions to participants or to facilitate tester interpretation of responses. Cultural reasons included modifications resulting from culturally inappropriate or unfamiliar content for the target culture(s). Linguistic reasons included modifications based on linguistic rules or naturalness of language in English. Language processing reasons included modifications to reflect similar language processing demands in English compared to French.

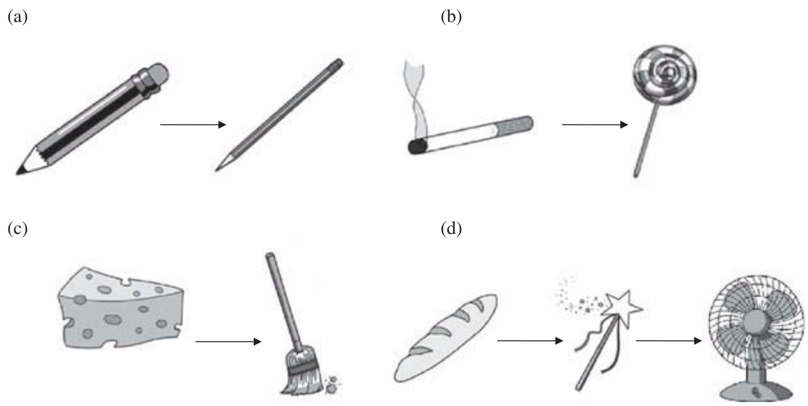

Figure 2. Administrative change in visual representation of pencil to a more stereotypical shape (a), cultural change from cigarette to lollipop (b), language change from French target and phonemic foil pair "cuillère/gruyère" (spoon/type of cheese) to English pair "spoon/broom" (c), and neuro-linguistic processing change for French target and phonemic foil pair "main/pain" (hand/bread) to "hand/wand", with subsequent decision to change "wand" to "fan", given more comparable semantic processing demands for the concepts "bread" and "fan" (d). Note that the items depicted illustrate the process of modifications and not necessarily the final selection of items for the English test.

Statistical analysis

Each unique item (n = 29) of the LAST-a and LAST-b comprised the unit of analysis. First, we evaluated agreement reliability among raters for difficulty and quality of the translations, using percentage agreement, where a 0–15 point difference constituted agreement (Bjorner, Thunedborg, Kristensen, Modvig, & Bech, 1998; Bullinger et al., 1998). Second, we computed univariate dispersion statistics for difficulty ratings, quality ratings, and testing results. Third, we evaluated group differences using the Kruskal–Wallis test for continuous variables and chi-squared analyses for frequency variables. We considered statistical significance to be alpha ≤0.05. Fourth, we recorded binary outcomes for problematic items, as modified (+) or unchanged (−), documenting the reasons for ensuing modifications. For statistical computations, we used SAS 9.2.

Results

Translation

The total number of proposed translations ranged from 1 to 12, 1 for items involving naming, single word repetition, and picture identification, and 12 for sentence repetition (item 7a) (Table 1). Overall, 17 of the 29 items had multiple proposed translations (Table 1), which the translators reconciled by consensus to produce adaptation I. For the naming subtest, translators identified between zero to five additional acceptable terms depending on the item, with a total of 19 additional acceptable terms across the LAST-a and LAST-b. For example, there were three acceptable additional terms for naming "television" including, "telly" (for speakers of British English) "TV", or "TV set". By comparison, the original French test allowed four additional acceptable terms for "télévision".

Table 1. Proposed translations and evaluations of the adapted items for the LAST-a and LAST-b.

Items	Proposed unique translations	Adaptation I evaluations		Adaptation II evaluations		Adaptation III evaluations	
LAST-a LAST-b	Total	Difficulty	Expert	Quality	Interviews	Expert	Testing
Oral expression							
Naming							
1a	1	–	–	–	–	–	–
1b	1	–	–	–	+	–	(+)
2a	1	–	–	–	–	–	–
2b	2	–	–	–	–	(+)	–
3a	1	–	–	–	–	+	–
3b	1	–	–	–	–	–	–
4a	1	–	–	–	–	–	–
4b	1	–	–	–	–	–	–
5a	1	–	–	–	–	–	–
5b	1	–	–	–	–	–	–
Repetition							
6a (word)	1	–	–	–	–	+	+
6b (word)	1	–	–	–	–	+	+
7a (sentence)	12[a]	+	+	(+)	–	+	–
7b (sentence)	11[a]	+	+	–	–	+	(+)
Automatic sequence							
8a and 8b	2	–	–	–	–	–	–
Auditory comprehension							
Picture ID (foil type)							
9a (phonemic)[c]	5[a]	+	–	–	–	+	–
9b (phonemic)[c]	4[a]	–	–	–	–	–	+
10a (phonemic)[d]	5[a]	+	–	–	–	+	–
10b (phonemic)[d]	3[a]	(+)	+	–	–	–	–
11a (semantic)	1	–	–	–	–	+	(+)
11b (semantic)	3[a]	–	–	–	–	–	–
12a (visual)	2[a]	(+)	–	–	–	–	(+)

(continued)

Table 1. (*Continued*).

Items	Proposed unique translations	Adaptation I evaluations		Adaptation II evaluations		Adaptation III evaluations	
LAST-a LAST-b	Total	Difficulty	Expert	Quality	Interviews	Expert	Testing
12b (visual)	2[a]	–	–	–	–	–	–
Commands							
13a (simple)	2	–	–	–	–	–	–
13b (simple)	2	–	–	–	–	–	–
14a (complex)	11[a]	+	+	–	+	–	–
14b (complex)	7[a]	+	+	(+)	+[b]	–	–
15a (two step)	3[a]	+	–	–	–	+	(+)
15b (two step)	2[a]	+	–	–	–	+	(+)
Items revised, *n*	**n/a**	**8**	**5**	**0**	**3**	**10**	**3**

Notes: – = Item not problematic.
+ = Item problematic and revised.
(+) = Item problematic, but not revised.
[a]Common translation across all three translators not proposed.
[b]Changed only to be parallel to LASTa sentence.
[c]Item with close phonemic foil (i.e., pair differed by one phoneme).
[d]Item with distant phonemic foil (i.e., pair differed by at least two phonemes).

Adaptation I evaluations

Reliability and consistency

Agreement reliability for difficulty ratings was 23/29 (79%). Difficulty ratings (median, interquartile range (IQR)) were low for items involving naming (0,0), word repetition (0,0), picture identification targets (0,3), and automatic sequence (0,6) and higher for those involving sentence repetition (33,22), picture identification foils (10,30), and commands (25,20) (Table 2). An example of an item with a rating of 0 across all three translators was the LAST-a naming item "pen". The item with highest ratings across all three translators was the LAST-b sentence repetition task with ratings of 40, 55, and 37. Mean difficulty scores per translator across all 29 items were 9.3 (*SD* 12.5, range 0–40), 11.4 (*SD* 17.3, range 0–55), and 11.4 (*SD* 14.4, range 0–40). Across subtests, mean ratings were 0.0 for naming, 2.0 for automatic speech, 16.1 for picture identification, 18.2 for repetition, and 21.5 for commands (mean of 12.7 for simple commands versus 31.7 for semi-complex and complex commands). Across all items, the mean difficulty ratings for the LAST-a and LAST-b were 11.0 and 9.8, respectively.

Modifications

Ten items had difficulty ratings above 25 for linguistic reasons, of which eight required modification (Table 1). The two unmodified items related to difficult foil choices. Based on expert panel review, five additional items required modification for linguistic (7a and 7b), administrative and linguistic (10b), and linguistic and language processing (14a and 14b) reasons (Table 1).

Adaptation II evaluations

Reliability and consistency

Percent agreement for the quality ratings was 85%, 93%, 90%, and 86% for clarity, common language, conceptual equivalence, and neurolinguistic equivalence, respectively. Quality ratings (median, IQR) were excellent for all four categories (100, 0) (Table 2).

Modifications

Two items had ratings below 75 involving sentence repetition (item 7a) and a complex command (item 14b) (Table 1). The two items remained unmodified, given irreconcilable morphosyntactic constraints between the English and French. Interviews resulted in no further additions of acceptable terms for the naming subtest. There was one error for the LAST-a two-step command (15a), where one participant completed the steps simultaneously, instead of sequentially. We modified the item for linguistic reasons along with its pair (15b), to maintain parallel structures for the LAST-a and LAST-b. We also modified one additional item (1b), due to incorrect naming with rapid self-correction on the part of two participants (given that self-correction ≤ 5 s constitutes a pass, the item was not actually in error), for administrative and cultural reasons (Table 1).

Adaptation III evaluations

Based on expert review, we reconsidered 11 items, modifying 10 (Table 1). Reasons for item modifications were cultural (item 11a), cultural and linguistic (item 3a), and

Table 2. Dispersion statistics for difficulty (n = 37) and quality ratings (n = 29) across translators.

	Rater 1	Rater 2	Rater 3	All raters
Difficulty[a], median (IQR), range	0 (20), 0–40	0 (22), 0–55	0 (20), 0–60	0 (20), 0–60
Quality[b], median (IQR), range				
Clarity	100 (0), n/a	100 (10), 90–100	100 (0), 80–100	100 (0), 80–100
Common language	100 (0), n/a	100 (0), 90–100	100 (0), 80–100	100 (0), 80–100
Conceptual equivalence	100 (0), 80–100	100 (0), 80–100	100 (0), 95–100	100 (0), 80–100
Neurolinguistic equivalence	100 (0), 80–100	100 (0), 60–100	100 (5), 80–100	100 (5), 60–100

Notes: In addition to the 29 items, the first three translators rated foils (n = 8) for difficulty. Where a translator proposed multiple translations for an item, average ratings were computed.
IQR = interquartile range.
[a]Translators 1, 2, 3.
[b]Translators 4, 5, 6.

Table 3. Aggregate raw frequencies for age, sex, education, and testing status for all participants (n = 109) by country.

	Australia (n = 34)	Canada (n = 25)	England (n = 20)	USA (n = 30)	p-Value
Age, median (IQR)	53 (26)	67 (27)	65 (31)	54 (20)	0.12
Female, n (%)	21 (62)	15 (60)	11 (55)	13 (43)	0.47
Secondary education, n (%)	31 (91)	25 (100)	19 (95)	30 (100)	0.19[a]
Postsecondary education, n (%)	21 (62)	18 (72)	11 (55)	24 (80)	0.23
Error rates in participants, n (%)	5 (15)	3 (12)	4 (20)	2 (7)	0.56

Note: IQR = interquartile range.
[a]50% of the cells in the chi-squared test had counts <5.

linguistic in the remaining eight (Table 1). We elected to retain one problematic item (item 2b) for further evaluation during pretesting.

Participants were comparable across countries, with no significant differences for age (p = 0.12), sex (p = 0.47), postsecondary education (p = 0.23), or errors (p = 0.56) (Table 3). Interviews resulted in a total of 22 acceptable terms across items for the naming subtest. There were four terms that were unique to a particular country, such as "pencil crayon" for "pencil" in Canada, and constituted a correct response if substituted for the target word. Conversely, short forms such as "croc" for crocodile were unacceptable, but a second attempt was permissible following examiner prompt to "say the whole word". Testing resulted in 15 errors by 14 participants for nine items overall (Table 1), with revisions to three items for administrative and linguistic reasons (items 6a, 6b, and 9b).

The three modified items involved single word productions by the examiner, revised to words that were more acoustically robust (i.e., involving fewer sounds subject to acoustic degradation from background noise or participant distance from the examiner). There were no errors during testing of revised items. We evaluated group differences for the remaining six items (involving 12 errors), finding no significant differences between participants with errors and those without for age (p = 0.79), sex (p = 0.39), or country (p = 0.48). However, there was a significant difference for postsecondary education (p = 0.04), whereby participants without postsecondary education made a greater number of errors.

Discussion

We were able to develop a new English tool that meets the current need for a linguistically valid and rapid aphasia screen for routine use after stroke. Consequently, we systematically followed previous guidelines for the adaptation and international harmonisation of tools (Acquadro et al., 2008; AERA, 1999; Bjorner et al., 1998; Bullinger et al., 1998; ITC, 2010; Jeanrie & Bertrand, 1999), but also developed new methods for adapting a language tool. Our multistep approach ensured continued evaluation of the linguistic properties of the original and target languages and demonstrated systematic methods to properly adapt a language test into a new language.

Translation of a health care tool involves a lengthy and complex process, but may still be more expedient than the development of a new tool. The eventual use of the same tools across cultures and/or linguistic contexts will increase identification of language impairment and foster international research aimed at optimizing aphasia management. During tool translation, it is advisable to undertake procedures as rigorous as those in the tool's initial development (Streiner & Norman, 2008). The International Test Commission also recommends that test adaptation take account of both linguistic and cultural differences (ITC, 2010). Multistep evaluation procedures, well delineated for patient-reported health questionnaires (Bullinger et al., 1998), should also apply to the adaptation and harmonisation of language tools in multinational trials (Acquadro et al., 2008).

To our knowledge, all previous endeavours to adapt the eight aforementioned aphasia screening tools into a new language are scarce and fail to provide comprehensive procedures for the linguistic adaptation (Košťálová et al., 2008; Mumby, 1988; Romero et al., 2012). Two studies adapted the MAST into Czech (Košťálová et al., 2008) and Spanish (Romero et al., 2012), while a third adapted the ASE (Reitan, 1985) into Panjabi (Mumby, 1988). The two adaptations of the MAST either lacked description of translation procedures (Košťálová et al., 2008) or failed to specify the number of translators or evaluation procedures (Romero et al., 2012). Although the adaptation of the ASE (Reitan, 1985) into Panjabi (Mumby, 1988) involved a comprehensive description of differing linguistic features between English and Panjabi, the actual translation procedures were unclear (Mumby, 1988). By using systematic multistep evaluations in conjunction with cross-linguistic comparisons, we ensured that LASTen assessed the same constructs as the original version (Ziegler & Bensch, 2013) and that it was suitable for multiple English dialects.

The development of the LASTen followed directly from the sequential stages of the adaptation process. For the translation, we provided instructions *a priori*, ensuring that translators optimise naturalness as well as linguistic comparability between the original French and their proposed English translations. Early and ongoing collaboration with the original tool developers was essential to replicate the linguistic constraints inherent in the original tool. For example, the French sentence repetition items involved a maximum of 11 syllables. To accommodate English morphological structure and rhythmic patterns for spoken language, translators allowed extra syllables in the sentence repetition task. Compared to French, English often requires a greater number of articulated (versus silent) verb tense and number morphemes (e.g., "he was going" versus "il allait") and fewer morphological concatenations of articles (e.g., "at the office" versus "au bureau"). Unstressed syllables or morphemes may also induce more rapidly produced speech in English (Frost, 2011). Consequently, allowance of extra syllables in English could ensure approximately equal relative length of production for the sentence repetition items.

Our process of sequential evaluations permitted qualitative reiterative discussion of potentially problematic items. Stage I evaluations of translation difficulty and expert panel review resulted in reconsideration of over one-third of the items. Likely due to the rigorous process of stage I evaluations, the subsequent stage II evaluations, quality evaluation and native speaker testing in Canada, revealed few additional problematic items. Only two items required modification, primarily to enhance clarity of administration. In fact, the two modifications resulted from a single error in performance of the two-step command in the LAST-a due to apparent simultaneous performance of the steps. The modification necessitated a parallel change to the LAST-b two-step command, despite the lack of error on this item. We chose to add the word "and" between the two steps of the command, to provide extra information pertaining to sequencing. The change from "then" to "and then" is consistent with natural and grammatical English syntax.

Evaluations for international harmonisation constituted stage III of the adaptation, emulating those from stage II, with expert review of the conceptual and linguistic constructs of the items followed by native speaker testing. Interestingly, the process of international harmonisation resulted in the greatest number of problematic items and consequent modifications compared to any other stage. Expert review was essential to ensure acceptability and naturalness of each item for all four dialects. An example of a discrepancy was a picture identification item “Show me the popsicle”. The term “popsicle” was not familiar to the English or Australian experts. Instead the term “ice lolly” was deemed more appropriate but was not familiar to the North American experts. Consequently, the proposed item and picture required modification to a new but similar concept, “ice cream”, to ensure equivalent terminology across dialects.

Healthy native speaker testing in the four countries further confirmed the linguistic suitability of the international adaptation of the LAST and provided a normative sample. As in the stage II healthy native speaker testing, errors provided the basis to potentially modify items for administrative reasons. Otherwise, errors permitted analysis of potential confounds, such as age, gender, country, or education level. Modifications for administrative reasons were necessary for three items, due to concerns of acoustic degradation of the examiner’s productions. Acoustic degradation can result from examiner distance, background noise, or physical interference with signal transmission, especially for phonemes such as voiceless fricatives. For example, the picture identification target “hat” along with its phonemic foil “cat” induced one error. Through careful review of the item and its foil, we noted a phonetic confound between the expression of the voiceless fricative /h/ and /k/ in word initial position. That is, the /k/ in “cat” involves an aspirated stop /k^h/, where its incorrect selection could easily ensue, especially if the /h/ in “hat” was not clearly audible. We elected to replace the /h/ in “hat” with a non-fricative word-initial phoneme. Still, we ensured that the phoneme /h/ was represented elsewhere in the LASTen, given its high frequency in English. Aside from modifications for administrative reasons, our native speaker testing provided a robust normative sample demonstrating comparable age, gender, and test performance across the four countries.

Evaluating a large sample of healthy participants establishes that a screening captures a normal function. When healthy participants fail to achieve ceiling, their test scores provide the basis from which to consider potential confounds. Of the existing aphasia screening tools designed for acute stroke, four lacked normative data (Azuar et al., 2013; Crary et al., 1989; Doesborgh et al., 2003; Thommessen et al., 1999), while the remaining four evaluated the performance of healthy native speakers (Enderby et al., 1987; Ernst, 1988; Flamand-Roze et al., 2011; Nakase-Thompson et al., 2005). The original LAST included a sample of 50 healthy native French speakers, who performed at ceiling (Flamand-Roze et al., 2011). Consequently, the pass cut-off for validation in stroke patients was performance >14/15, where an inaccurate response on any given item constituted failure (Flamand-Roze et al., 2011).

Normative sampling for the MAST included 36 healthy native speakers (Nakase-Thompson et al., 2005). Participants performed close to ceiling (mean of 9.9/10) on all tasks, except for verbal fluency (mean of 6.4/10) (Nakase-Thompson et al., 2005). There were significant correlations between fluency subtest scores and age and between years of education and expressive index scores (Nakase-Thompson et al., 2005). Overall, the study lacked a proposal for cut-off scoring. Normative sampling for the ASE involved 85 healthy older participants, 65–75 years of age, with a proposed cut-off of 25/32 (Ernst, 1988). There were significant differences for performance only according to education level (Ernst, 1988).

The FAST has undergone two evaluations in healthy participant groups (Enderby et al., 1987; O’Neill, Cheadle, Wyatt, McGuffog, & Fullerton, 1990). The first study evaluated performance in 123 participants, with ages ranging from 20 to over 81 years (10 participants were ≥81 years) (Enderby et al., 1987). Performance differed according to age stratifications, with proposed cut-offs of >27/30 for participants 20 to 60 years and >25/30 for participants ≥61 years (Enderby et al., 1987). The second study evaluated 51 older healthy native speakers ranging from 69 to 90 years (O'Neill et al., 1990). It provided evidence for a new cut-off of >23/30 (O'Neill et al., 1990), which was in keeping with the performance-derived cut-offs from the initial validation in stroke patients (Enderby et al., 1987). Neither study documented education levels of participants; therefore, the potential confound of education level remains undetermined.

Like the original LAST, the LASTen demonstrated performance close to or at ceiling during healthy participant testing. However, 10% of our participants made a single error on unrevised items. Unlike the MAST (Nakase-Thompson et al., 2005) and the FAST (Enderby et al., 1987), the LASTen lacked significant differences across age groups, likely reflecting the dedicated effort during test development to restrict cognitive processing demands to language. Similar to the MAST (Nakase-Thompson et al., 2005) and the ASE (Frost, 2011), our error rates differed significantly by level of education. Because of the discrepancy in error rates between those with and without postsecondary education, we suggest further consideration of cut-off thresholds or scoring procedures during validation in stroke patients. For example, it may be necessary to lower the threshold of pass from >14 points to >13 in those without postsecondary education. Alternatively, adding a point to the final score for those without postsecondary education may constitute an adequate means to account for education level, comparable to the scoring system of the Montreal Cognitive Assessment (Nasreddine et al., 2005).

Our adaptation and international harmonisation of LASTen had some limitations. First, translation requires subjective determination of linguistic modifications that are in keeping with "naturalness" of the target language. Consequently, translation of a language tool requires comprehensive knowledge of differing cross-linguistic constraints that might affect natural performance in the target language. We addressed limitations in the translation process by developing a translation manual to guide translator decisions regarding linguistic comparability of French and English. We then conducted multiple sequential evaluations to ensure the quality of the adaptation, finally testing a normative sample of healthy native speakers, to confirm both naturalness and linguistic validity.

Second, although we conducted testing in four countries, we did not sample regional variation within countries. However, dialectal variation occurring at the phonetic level is not of chief concern in language testing, because it relates primarily to speech execution. Still, we carefully considered phonotactic constraints within dialects. For example, we allowed the term "ink pen" as a response to the naming item "pen", because in some regional American dialects the vowel in "pen" is commonly raised to "pin". Consequently, some Americans may routinely use the term "ink pen" to distinguish "pen" from "pin" (Baranowski, 2013).

Third, we relied on convenience sampling in the four English speaking countries. However, we attempted to recruit participants with a mean age similar to that of stroke patients in each country, with comparable gender frequencies and education levels. Our group comparisons demonstrated that across countries the samples were comparable for age, gender, education, and error rates. Although our final sample of participants had a lower mean age than that of stroke patients in the four countries (Canadian Stroke Network, 2011; Hankey et al., 2000; Lee et al., 2011; Petrea et al., 2009), it compared well to the stroke sample in the original French validation (60 versus 63 years of age, respectively) (Flamand-Roze et al., 2011).

Finally, we limited normative testing to healthy native speakers of English within the four countries. Accordingly, we recorded information on age, gender, education level, and participant report of health history pertinent to language testing, but could not evaluate other potential confounds. Our testing could not account for language proficiency or potential concomitant cognitive or motor deficits. Still, the information we collected permitted confirmation of equivalent gender, age, and education level statistics across the four countries.

The current study has provided rigorous and reproducible methods to promote and facilitate future endeavours in the translation of language tools. Clinicians and researchers can replicate the same process by (1) using translation methods that optimise both linguistic comparability and naturalness, (2) repeatedly reviewing translation quality and corresponding content validity through multiple evaluations, and (3) establishing linguistic sensibility and normative performance through native speaker testing. The comprehensive methodological procedures in our adaptation and international harmonisation of LASTen will promote comparable psychometric properties to the original LAST when validated in stroke patients. We now plan to validate the internationally harmonised LASTen in consecutive stroke patients from all four countries, to confirm or further modify adaptation IV for routine use in cross-cultural contexts (Ziegler & Bensch, 2013). Once validated in stroke patients, LASTen will provide an optimal opportunity to facilitate the development of clinical paradigms for the identification and management of aphasia. It will also provide the means to conduct future cross-linguistic and international patient-oriented research (Pollock et al., 2012).

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Disclosure statement

No potential conflict of interest was reported by the authors.

Note

1. The term British English refers to our capture of common dialectal features in England. Examples provided may not reflect similar linguistic phenomena in other dialects of British English across the United Kingdom.

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Exploitation des résultats :

Processus d'adaptation en anglais publiée dans **Aphasiology (Impact Factor : 1.7)**

Adaptation en Québécois publié dans **La Revue Neurologique (Impact Factor** : 0.5)

Présentations dans des congrès nationaux et internationaux :

Adapter une échelle de langage (LAST : *language screening test)* du français à l'anglais : un challenge ! H. Flowers, **C. Flamand-Roze**, E. Roze, S. Skore, C. Sénal, C. Denier, R. Martino. (Communication affichée. Journées de neurologie de langue française. Montpellier 2013)

Adapting the Language Screening Tool (LAST) from French into English: Aphasia screening after stroke. Heather L. Flowers , **Constance Flamand-Roze,** Christian Denier, Emmanuel Roze, Frank L. Silver, Elizabeth Rochon, Stacey A. Skoretz, Rosemary Martino. (Présentation affichée Canadian Stroke Congress 2012).

LAST-Q: Adaptation and normative data for the Language Screening Test in a French-Canadian population L. Monetta, J.Bourgeois-Marcotte, **C. Flamand-Roze**, C. Denier (Communication affichée. 52nd Annual Meeting of the Academy of Aphasia Miami 2014)

LAST-Q: Adaptation and normative data for the Language Screening Test in a French-Canadian population. L. Monetta, J. Bourgeois-Marcotte, **C. Flamand-Roze**, C. Denier. (8e Journée de la recherche en neurosciences de l[1]Université Laval, Québec, Canada.)

International Harmonization and Pilot Testing of the English Language Screening Test (LAST) : Heather L. Flowers , **Constance Flamand-Roze,** Emmanuel Roze, Frank L. Silver, Elizabeth Rochon, Stacey A. Skoretz, Rosemary Martino. (Présentation affichée Canadian Stroke Congress 2014).

Aphasie et troubles moteurs dans les AVC ; quelle évolution précoce en suite de thrombolyse ?

Les patients présentant une aphasie à la suite d'un AVC peuvent garder des séquelles à long terme, même si le score NIHSS initial était bas. Toutefois, une récupération spectaculaire peut être constatée chez les patients ayant bénéficié d'un traitement par thrombolyse.

Les descriptions de l'évolution précoce des troubles phasiques après thrombolyse sont peu nombreuses, en particulier en comparaison à celles des troubles moteurs. Il nous a semblé important d'étudier en détail une large population de patients ayant bénéficié d'un traitement par thrombolyse afin d'avoir une idée précise de l'évolution précoce de l'aphasie dans les AVC, qu'elle soit associée ou non à un trouble moteur.

Fiche de recherche:
Rôle : co-investigateur principal. Recueil des données, analyse des résultats, rédaction et soumission de l'article.
Equipe de recherche : Dr C. Denier (INSERM U788), Dr E. Roze (INSERM U952, CNRS U7224 UPMC Paris 6), Pr D. Ducreux, Pr F. Picot
Nombre de patients : 338
Type de recherche : étude de cohorte.
Sites : CHU Bicêtre USINV- CHG de Versailles-Mignot

Méthodes :

Les données démographiques, cliniques et radiologiques des patients thrombolysés de 2 USINV (Bicêtre, Versailles) ont été colligées pendant 5 ans. La récupération globale a été mesurée par le score NIHSS à l'entrée, H24 (un jour après l'AVC) et J8 (à une semaine de l'AVC) afin de quantifier l'évolution précoce. Les patients étaient considérés comme aphasiques si l'item 9 (langage) du NIHSS était supérieur à 0, ce qui correspond à la présence d'un trouble du langage (un score de 0 étant considéré comme un absence de déficit). Nous avons utilisé des scores composites : moteurs (items 4,5 et 6 du NIHSS) et langage (items 1b, 1c et 9) afin de comparer l'évolution des deux déficits.

Résultats :

Sur 338 patients ayant bénéficié de la thrombolyse, 137 (40,5 %) ont présenté une aphasie. Cent neuf présentaient une aphasie associée à un déficit moteur. Il n'y a pas de différence de fréquence de normalisation des scores composites moteurs/langage à H24 (14,6 %/16,5 %) ni à J8 (32,1 %/ 37 %). Toutefois, l'aphasie récupère significativement plus quand le déficit du langage est isolé (28 patients), avec $p < 0,05$ à H24 et $p < 10^{-4}$ à j8.

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Aphasia in stroke patients: early outcome following thrombolysis

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Background: Data on the early course of stroke-related aphasia after thrombolysis are scant.
Aims: The aim of this study was to describe recovery patterns of aphasia after thrombolysis in a large sample of stroke patients.
Methods & Procedures: Clinical and radiological data of consecutive stroke patients treated with thrombolysis over a 5-year period were routinely entered into prospective registries at two stroke units. Recovery was evaluated using the National Institutes of Health Stroke Scale (NIHSS) at baseline, after 24 hr, and on day 7. Aphasia was defined as a score >0 on item 9 of the NIHSS (measurement of language skills), aphasia improvement as any decrease in the item-9 score, and aphasia resolution as an item-9 score of 0. To assess global motor and language impairments, we created a composite language score obtained by summing the scores for items 1b, 1c, and 9; and a composite motor score obtained by summing the scores for items 4, 5, and 6.
Outcomes & Results: Out of the 338 patients treated with thrombolysis, 137 (40.5%) had aphasia. In patients with both aphasia and motor deficits (n = 109), these two impairments showed similar recovery patterns. Aphasia recovered significantly better in patients without limb motor deficits (n = 28) than those with limb motor deficits (n = 109), both after 24 hr ($p < 0.05$) and after 7 days ($p < 0.0001$). These results were supported by findings from a group-based trajectory modelling methods ($p < 0.005$).
Conclusions: Language impairments and limb motor deficits show similar recovery after thrombolysis in a given patient. Aphasia recovery is significantly better in the absence of limb motor deficits.

Keywords: aphasia; stroke; thrombolysis; language; dramatic recovery

Introduction

At the acute stage of stroke, the frequency of language disorders has varied widely across studies, from 15% to 40% (Croquelois & Bogousslavsky, 2011; Engelter et al., 2006; Godefroy, Dubois, Debachy, Leclerc, & Kreisler, 2002; Inatomi et al., 2008; Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001; Maas et al., 2012; Pedersen, Jørgensen, Nakayama, Raaschou, & Olsen, 1995). These discrepancies are probably ascribable to the lack of sensitive and suitable tools for assessing aphasia at the bedside as well as to

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differences in the time from stroke onset to aphasia evaluation. Recovery from stroke-related aphasia remains difficult to predict. Reported prognostic factors include age, initial stroke and aphasia severity as assessed using the National Institutes of Health Stroke Scale (NIHSS), the phonology score, the Barthel index, and stroke subtype (El Hachioui et al., 2013; Inatomi et al., 2008; Lazar et al., 2010; Lazar, Speizer, Festa, Krakauer, & Marshall, 2008; Pedersen, Vinter, & Olsen, 2004). Despite a potential for rapid improvement, language impairments persist 18 months after the stroke in 50% of patients with aphasia (Pedersen et al., 2004). Aphasia due to ischaemic stroke is considered to have a low likelihood of recovery (Croquelois & Bogousslavsky, 2011; Godefroy et al., 2002; Pedersen et al., 2004). Patients with stroke-related aphasia may remain disabled for several years, even when their initial NIHSS score was low. Residual aphasia is often associated with depression, limited investment in the rehabilitation process, difficulty understanding therapists' instructions, social withdrawal, and low rates of work resumption. As a result, both quality of life and the ability to engage in everyday activities are substantially impaired (Basso, 1992; Black-Schaffer & Osberg, 1990; Kauhanen et al., 2000; Kremer, Perren, Kappelin, Selariu, & Abul-Kasim, 2013; Nesi, Lucente, Nencini, Fancellu, & Inzitari, 2014).

Dramatic recovery of stroke-related impairments after recanalisation was reported recently. The degree of recovery may constitute a good predictor of the long-term outcome (Alexandrov et al., 2000; Blinzler et al., 2011; Felberg et al., 2002; Mikulik et al., 2010). Few studies have focussed on the early course of aphasia after thrombolysis, and it is unclear whether the recovery time-course is similar for aphasia and limb motor deficits (Felberg et al., 2002; Kremer et al., 2013; Lazar et al., 2010; Leira, Ludwig, Gurol, Torner, & Adam, 2012; Mikulik et al., 2010).

Here, we report the early outcome of aphasia 24 hr (H24) and 7 days (D7) after thrombolysis in consecutive patients with ischaemic stroke admitted to two stroke units over a 5-year period.

Patients, material, and method

Whole cohort

We prospectively enrolled consecutive patients with ischemic stroke treated with thrombolysis over a 5-year period at two stroke units in France (Versailles, 2006–2011; Bicêtre, 2007–2012). Patients eligible for conventional intravenous thrombolysis received the standard dose of recombinant tissue-type plasminogen activator within 4.5 hr after stroke onset in compliance with guidelines (National Institute of Neurological Disorders and Stroke (NINDS), 1995; Hacke et al., 2004). Patients with a documented arterial occlusion who had contraindications to intravenous treatment were managed with intra-arterial mechanical thrombectomy. The diagnosis of ischaemic stroke was confirmed by magnetic resonance imaging (MRI) if possible and by computed tomography (CT) when MRI was contraindicated. The aetiological work-up routinely included cervical and trans-cranial Doppler, echocardiography, and electrocardiogram monitoring for at least 48 hr. Additional investigations were performed as appropriate (e.g., laboratory tests, lumbar puncture, trans-oesophageal echocardiography, and cerebral angiogram). Aetiologies were classified according to both the Trial of Org 10,172 in Acute Stroke Treatment classification and the involved vascular territories as assessed by brain imaging. MRI or CT was repeated 24 hr after treatment onset to detect haemorrhagic complications. Symptomatic haemorrhage was defined as a combination of neurological status deterioration and new evidence of bleeding by brain imaging.

1a—Level of consciousness	0 = Alert; keenly responsive 1 = Not alert, but arousable by minor stimulation 2 = Not alert; requires repeated stimulation 3 = Unresponsive or responds only with reflex
1b—Level of consciousness questions: What is your age? What is the month?	0 = Answers two questions correctly 1 = Answers one question correctly 2 = Answers neither questions correctly
1c—Level of consciousness commands: Open and close your eyes Grip and release your hand	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly
2—Best gaze	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation
3—Visual	0 = No visual lost 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia
4—Facial palsy	0 = Normal symmetric movements 1 = Minor paralysis 2 = Partial paralysis 3 = Complete paralysis of one or both sides
5—Motor arm Left arm Right arm	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement
6—Motor leg Left leg Right leg	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement
7—Limb ataxia	0 = Absent 1 = Present in one limb 2 = Present in two limbs
8—Sensory	0 = Normal; no sensory loss 1 = Mild-to-moderate sensory loss 2 = Severe-to-total sensory loss
9—Best language	0 = No aphasia; normal 1 = Mild-to-moderate aphasia 2 = Severe aphasia 3 = Mute; global aphasia
10—Dysarthria	0 = Normal 1 = Mild-to-moderate dysarthria 2 = Severe dysarthria
11—Extinction and inattention	0 = No abnormality 1 = Visual, tactile, auditory, spatial, or personal inattention 2 = Profound hemi-inattention or extinction
Score = 0–42	

Figure 1. The National Institutes of Health Stroke Scale (NIHSS).
Note: NIHSS is a systematic assessment tool that provides a quantitative measure of stroke-related neurological impairments.

For each patient, the following characteristics were recorded prospectively: age, gender; handedness; first language; history of hypertension, diabetes mellitus, dementia, and/or stroke; smoking history; time from symptom onset to thrombolysis initiation; stroke signs and clinical severity based on the NIHSS (Figure 1); involved vascular territories; and aetiology. The NIHSS is used in acute stroke to objectively quantify the stroke-related impairments. Each of the 11 items assesses a specific ability and is scored from 0 to 2, 3, or 4. For each item, a score of 0 typically indicates normal function in that specific ability and higher scores greater levels of impairment. The maximum possible score is 42. Three items reflect language processing abilities, namely, 1b, answering questions; 1c, understanding commands; and 9, language expression (naming objects pictured on cards, reading sentences, and describing what is happening in a picture). The patient can answer in writing. Item 9 is specifically designed to assess aphasia; a score of 0 indicates normal speech; 1, mild-to-moderate aphasia; 2, severe aphasia; and 3, an inability to speak or to understand speech. Thus, the scoring of item 9 requires experience on the part of the physician. In our study, patients were evaluated by trained physicians who were able to distinguish aphasia from other disorders such as apraxia of speech and dysarthria. In doubtful cases, two experienced speech therapists (CFR and MS) evaluated the patient to determine the correct score.

Aphasic patients

Aphasia was diagnosed when the initial score on NIHSS item 9 was greater than 0 and was always confirmed by an experienced speech therapist (CFR or MS). We classified patients with aphasia into two groups based on whether they had a limb motor deficit, defined as a score greater than 0 on NIHSS items 5 and/or 6 (A group and A + M group, respectively). Isolated aphasia was defined as a score greater than 0 on NIHSS item 9, with or without scores greater than 0 on items 1b and 1c, and with scores of 0 on all other items.

Aphasia recovery

- Aphasia improvement was defined as any decrease in the item-9 score and aphasia recovery as an item-9 score of 0.
- We created two composite scores to evaluate and monitor global motor and language impairments: the composite language score was obtained by summing the scores on items 1b (questions), 1c (commands), and 9 (language) and the composite motor score by summing the scores on items 4 (facial palsy), 5 (motor arm), and 6 (motor leg). We computed both the total scores and the percentages of score decreases between time points.

We evaluated functional recovery using the NIHSS items at baseline, then at H24 and at D7 after thrombolysis. Dramatic recovery was defined as an NIHSS score decrease ≥10 points within 24 hr (Alexandrov et al., 2000; Felberg et al., 2002). Patients with aphasia received daily speech and language therapy (SLT) from baseline to discharge when appropriate.

Statistical analysis

Means, standard deviations, medians, and ranges were computed for continuous variables and frequencies and chi-square values for categorical variables. Fisher's exact test was used when fewer than five values were expected for any cell. For comparisons, the statistical significance of observed differences was evaluated using rank tests for non-normally distributed variables and parametric tests for normally distributed variables, with $p < 0.05$ taken to indicate statistical significance. All statistical analyses were performed using SAS software version 9.3 (SAS Institute, Cary, NC, USA) and R software version 2.13.1 (www.r-project.org/). Trajectories were identified using the KmL package in R and the Proc Traj procedure in SAS (Genolini & Falissard, 2011; Jones, Nagin, & Roeder, 2001).

Evolution of motor and language deficits following thrombolysis

Assessing changes in composite scores within the entire cohort would have been irrelevant, since overlap occurred between the A and M groups and the A + M group. We therefore described:

- First, the outcomes in the entire cohort
- Second, the language and motor outcomes in the A + M group
- Third, the aphasia outcomes in the A + M and A groups

Association between longitudinal aphasia outcomes after thrombolysis and leg/arm motor deficit at admission

To evaluate potential associations linking aphasia outcomes after thrombolysis and limb motor deficits at baseline, we used group-based trajectory modelling. This method relies on a statistical tool (the KmL function of R) to detect groups of patients who share the same pattern of change over time. This tool corresponds in practice to a K means algorithm adapted to longitudinal data. As with all cluster analysis procedures, the robustness of the results obtained using KmL must be assessed. To this end, we used the Proc Traj of SAS, which determines mixtures of longitudinal data. Results were similar with both methods, indicating that the partition obtained using KmL was robust. We preferred KmL over Proc Traj for the final results because KmL provides nonparametric trajectories, which is not the case with Proc Traj. A censored normal distribution was used to model composite language score data. The partition with the highest Calinski & Harabatz criterion value was selected. Trajectories were identified using the KmL package of R (Genolini & Falissard, 2011) and the Proc Traj procedure of SAS (Jones et al., 2001). The strength of the association between presence of a limb motor deficit and trajectory findings was evaluated using the chi-square test. We also compared aphasia trajectories across different variables (H24 and D7 evaluations, time to thrombolysis, and clinical and demographic variables) (Genolini & Falissard, 2011; Jones et al., 2001).

Results

Baseline characteristics of the whole cohort

During the 5-year study period, 338 consecutive patients with ischemic stroke were treated with thrombolysis (n = 166 in Bicêtre and n = 172 in Versailles), including 41 using intra-arterial procedures. Baseline characteristics and main risk factors were not significantly different between the populations from the two centres, which were therefore pooled (data not shown). Mean age was 68.9 ± 15.2 years and 55% of patients were male. Table 1 reports the topographic distribution. The mean NIHSS score at baseline was 13.8 overall and was higher in the group with left hemispheric than with right hemispheric involvement (Table 1, p < 0.001, Student's t-test). Median time from stroke onset to thrombolysis was 180 min overall.

Characteristics of patients with or without aphasia

Of the 338 patients, 137 (40.5%) had aphasia at admission. Among them, 129 (94.2%) had left middle cerebral artery (MCA) infarction. The remaining eight patients had right MCA infarction; four of them were bilingual with acquisition of French as their second language at the age of 6 years (n = 2), 20 years (n = 1), and 30 years (n = 1), and another had a history of left MCA infarction with aphasia followed by a full recovery, according to his speech therapist. Table 2 reports the baseline characteristics of patients with and without aphasia. The only significant difference was a higher mean baseline NIHSS score

Table 1. Baseline characteristics of the patients with ischaemic stroke treated with thrombolysis.

	Left anterior hemispheric infarction (MCA/AChA) (n = 139, 41.1%)	Right anterior hemispheric infarction (MCA/AChA) (n = 178, 52.7%)	Vertebro-basilar infarction (PCA/basilar) (n = 21, 6.2%)	Total (n = 338)
Males/females, n (%)	72/67 (52/48)	98/80 (55/45)	16/5 (76/24)	186/152 (55/45)
Age (years), mean ± SD (median)	67.1 ± 14.9 (69.5)	69.9 ± 15.5 (73)	69.4 ± 14.6 (70)	68.9 ± 15.2 72)
French as first language, n (%)	117 (84)	Not routinely recorded	20/21 (95)	
French as second language, n (%)	19 (13)		1 (5)	
No knowledge of French	3 (2)		0 (0)	
Hypertension, n (%)	81 (58.3)	108 (60.7)	7 (33.3)	196 (58.0)
Diabetes mellitus, n (%)	23 (16.5)	26 (14.6)	8 (38.1)	57 (16.9)
Tobacco use, n (%)	33 (23.7)	35 (19.7)	6 (28.6)	70 (20.7)
Hyperlipidaemia, n (%)	52 (37.4)	67 (37.6)	8 (38.1)	127 (37.6)
Atrial fibrillation, n (%)	44 (31.6)	67 (37.6)	2 (9.5)	113 (33.4)
NIHSS before thrombolysis, mean ± SD (median)	15.6 ± 6.6 (17.5)	12.9 ± 5.1 (13)	9.5 ± 5.6 (8)	13.8 ± 6.0 (14)
Time from onset to thrombolysis (minutes), mean ± SD (median)	178 ± 70 (172.5)	180 ± 49 (180)	183 ± 32 (180)	179 ± 58 (180)

Notes: MCA, middle cerebral artery; AChA, anterior choroidal artery; PCA, posterior cerebral artery; NIHSS, National Institutes of Health Stroke Scale.

Table 2. Baseline characteristics of patients with and without aphasia.

	Aphasia (item 9 > 0) (n = 137)	No aphasia (item 9 = 0) (n = 201)	Total (n = 338)
Males/females, n (%)	75/62 (55/45)	111/90 (55/45)	186/152 (55/45)
Age (years), mean ± SD (median)	67.9 ± 14.7 (71.0)	69.4 ± 15.1 (73.0)	68.8 ± 150 (72.0)
Risk factors, n (%)			
High blood pressure	80 (59.3)	116 (57.7)	196 (59.9)
Diabetes mellitus	21 (15.7)	36 (17.9)	57 (17.4)
Tobacco use	31 (22.8)	39 (20.6)	70 (21.5)
Hyperlipidaemia	53 (40.5)	74 (36.8)	127 (39.8)
Atrial fibrillation	46 (33.6)	67 (33.3)	113 (33.4)
Baseline NIHSS score, mean ± SD (median)	16.0 ± 6.6* (18)	12.3 ± 5.1* (12)	13.8 ± 6.0 (14)
Time from onset to thrombolysis (minutes), mean ± SD (median)	180 ± 72 (180)	179 ± 45 (180)	179 ± 58 (180)

Note: *$p < 10^{-5}$ by Student's t-test.

in the group with aphasia ($p < 10^{-5}$, Student's t-test). Of the 137 patients with aphasia, 109 had limb motor deficits (A + M group) and 28 did not (A group).

Global outcome after thrombolysis

Table 3 reports the global NIHSS scores at baseline, H24, and D7 as well as outcomes according to the vascular territories involved or presence of aphasia. Dramatic recovery occurred in 72 (21.3%) of the 338 patients, including 32 with left MCA infarctions, 35 with right MCA infarctions, 4 with vertebro-basilar (VB) infarctions, and 1 with an anterior choroidal artery infarction. Of the 137 patients with aphasia, 35 (10.3%) achieved

Table 3. Recovery according to arterial territories or presence of aphasia.

	Baseline NIHSS, mean ± SD (median)	H24 NIHSS, mean ± SD (median)	D7 NIHSS mean ± SD (median)
Total (n = 338)	13.8 ± 6.0 (14)	8.6 ± 7.1 (7)	6.1 ± 6.7 (4)
According to vascular territory involved			
Left anterior hemispheric infarction (MCA/AChA) (n = 139)	15.6 ± 6.6 (17.5)	9.7 ± 7.3 (8)	6.5 ± 7.2 (3)
Right anterior hemispheric infarction (MCA/AChA) (n = 178)	12.9 ± 5.1 (13)	8.1 ± 6.8 (7)	5.6 ± 6.0 (4)
Vertebro-basilar infarction (PCA/basilar) (n = 21)	9.5 ± 5.6 (8)	5.1 ± 6.1 (3.5)	6.2 ± 7.3 (6)
According to presence of aphasia			
Aphasia (item 9 > 0) (n = 137)	16.0 ± 6.6 (18)*	10.1 ± 7.4 (8)	6.8 ± 7.1 (4)
No aphasia (item 9 = 0) (n = 201)	12.3 ± 5.1 (12)*	7.6 ± 6.7 (5.5)	5.5 ± 6.2 (4)

Notes: *$p < 10^{-5}$ by Student's t-test. NIHSS, National Institutes of Health Stroke Scale; MCA, middle cerebral artery; AChA, anterior choroidal artery; PCA, posterior cerebral artery.

a dramatic recovery, including 32 with left MCA and 3 with right MCA infarction. Intracerebral haemorrhage was seen on the routine neuroimaging study at H24 in 29.9%, with no significant difference between the groups with right and left anterior hemispheric infarcts or between the groups with and without aphasia (data not shown). Symptomatic intracerebral haemorrhage occurred in 9 (2.7%) patients. Overall, D7 mortality was 38/338 (11.2%) (11 patients with left MCA, 23 with right MCA, and 4 with VB infarctions). D7 mortality in the group with aphasia (6/137, 4.4%) was lower than in the overall cohort; D7 mortality was 5/109 (4.5%) in the A + M group and 1/28 (3.5%) in the A group. Table 3 reports the recovery data in groups defined based on vascular territory involved and on presence of aphasia.

Recovery after thrombolysis

Patients with aphasia (n = 137) with or without limb motor impairment

At H24, the composite language score was improved in 85 (62.0%) of the 137 patients with aphasia, unchanged in 41 (30.0%), and worsened in 10 (7.2%); 1 patient died before H24. Corresponding values on D7 were 110 (81.1%), 17 (12.4%), and 8 (5.8%); an additional patient died between H24 and D7. The mean decrease in the composite language score was 32.7% at H24 and 58.5% on D7. Language returned to normal in 14.6% of patients by H24 and 32.1% by D7. The limb motor deficit resolved fully by H24 in 18 (16.5%) patients and by D7 in 40 (37.0%).

Patients with aphasia and limb motor deficits (A + M group, n = 109)

In the 109 A + M patients, no significant differences were found between recovery of language and recovery of motor function at H24 or on D7. At H24, the composite language score was improved in 67 (61.5%) A + M patients, unchanged in 36 (33.0%), and worsened in 6 (5.5%). Corresponding values on D7 were 90 (82.5%), 16 (14.7%), and 3 (2.8%). At H24, the composite motor score was improved in 86 (78.9%) A + M patients, unchanged in 18 (16.5%), and worsened in 5 (4.6%). On D7, corresponding values were 89 (81.6%), 16 (14.7%), and 4 (3.7%) ($p = 0.86$). At H24, the language and limb motor deficit NIHSS scores were normal (equal to 0) in 12 (11.0%) and 15 (13.8%) patients, respectively ($p = 0.53$). Corresponding values on D7 were 31 (28.4%) and 34 (31.2%) ($p = 0.66$).

Patients with dramatic recovery of aphasia (n = 35)

Among patients with dramatic recovery of aphasia, 97.0% showed improvement of the composite language score by H24 and 100% by D7. Full aphasia recovery was achieved by 20.0% of these patients by H24 and 40.0% by D7. Corresponding values for full limb motor deficit recovery were 20.0% and 48.6% (NS).

Patients with aphasia and no limb motor deficits (A group; n = 28)

Aphasia with no limb motor deficit occurred in 28 patients, i.e., 8.3% of the entire cohort and 20.4% of patients with aphasia (Table 4). This group had significantly better aphasia outcomes compared to the other patients, with mean decreases in the composite language score of 43.1% by H24 ($p = 0.001$) and 80.6% by D7 ($p < 0.0001$) versus 29.9% and

Table 4. Aphasia recovery at H24 and D7 following thrombolysis in patients with and without limb motor deficits.

	No limb motor deficit (*n* = 28)	Limb motor deficit (*n* = 109)	All patients with aphasia (*n* = 137)	*p*-Value
Age (years), mean ± SD	67.2 ± 14.2	67.2 ± 14.7	67.2 ± 14.7	
Before treatment				
NIHSS score, mean ± SD	6.8 ± 1.9	18.3 ± 5.2	16.0 ± 6.6	$p < 0.0001$
Item-9 score, mean ± SD	2.1 ± 0.7	2.5 ± 0.7	2.4 ± 0.7	$p = 0.2$ (NS)
Composite language score (items 1b + 1c + 9), mean ± SD	4.3 ± 1.6	5.1 ± 1.8	4.9 ± 1.7	$p = 0.15$ (NS)
24 hr after treatment				
NIHSS score, mean ± SD	4.0 ± 3.8	11.7 ± 7.2	10.1 ± 7.3	$p < 0.0001$
Item-9 score, mean ± SD	1.3 ± 1.1	1.9 ± 1.0	1.8 ± 1.1	$p < 0.001$
Composite language score (items 1b + 1c + 9), mean ± SD	2.5 ± 2.2	3.6 ± 2.3	3.4 ± 2.3	$p = 0.025$
% decrease in composite language score (baseline-H24)/baseline	43.1% ± 49.3%	29.9% ± 38.6%	32.7% ± 41.3%	$p = 0.001$
7 days after treatment				
NIHSS score, mean ± SD	1.4 ± 1.8	8.3 ± 7.4	6.8 ± 7.2	$p < 0.0001$
Item-9 score, mean ± SD	0.6 ± 0.6	1.4 ± 1.1	1.2 ± 1.1	$p < 0.0001$
Composite language score (items 1b + 1c + 9), mean ± SD	0.9 ± 1.1	2.6 ± 2.4	2.2 ± 2.2	$p < 0.0001$
% decrease in composite language score (baseline-D7)/baseline	80.6% ± 25.1%	52.4% ± 40.4%	58.5% ± 39.3%	$p = 0.0001$

52.4%, respectively, among the 109 A + M patients. Although both the mean item-9 score and the mean composite language score were similar at baseline in the two groups, both scores were significantly lower in the A than in the A + M group by H24 ($p < 0.05$) and D7 ($p < 0.0001$) (Table 4).

Isolated aphasia (n = 1)

Only 1 (0.3%) of the 338 patients had strictly isolated aphasia defined as scores of 0 on all items except 9, 1b, and 1c. Three other patients had dysarthria (item 10 > 0) in addition to aphasia. None of these four patients achieved full aphasia recovery by D7, despite low baseline values of the total NIHSS score.

Group-based trajectory modelling

The group-based trajectory modelling method was used to study the pattern of changes of aphasic symptoms following thrombolysis. Results are illustrated in Figure 2. The partitionings independently found using SAS and KmL software were very close. By means of software, an optimal solution for a partition into four groups was found (groups 1, 2, 3, and 4 shown in Figure 2). Eleven percent of the patients were classified as having an

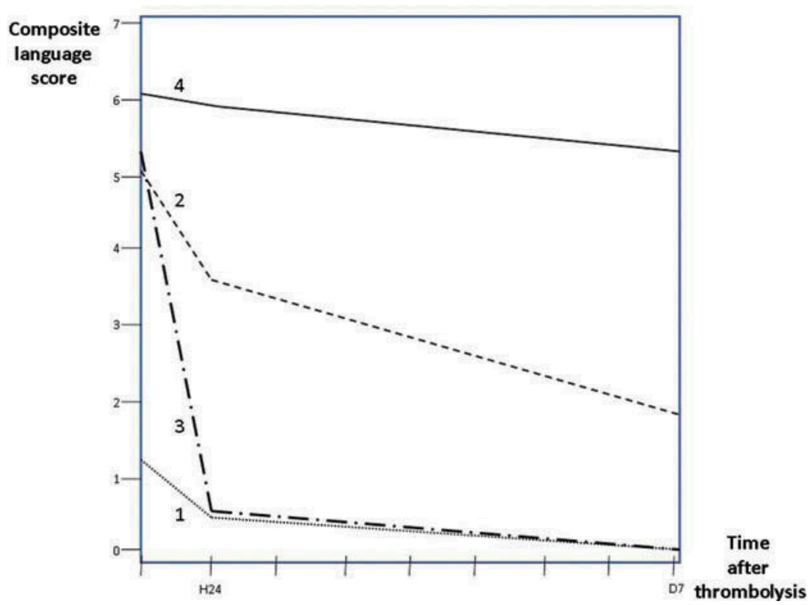

Figure 2. Group-based trajectory modelling: optimal solution for categorising patients based on the time-course of aphasia after thrombolysis.
Notes: Group-based trajectory modelling using KmL software was used to study the pattern of change in aphasia after thrombolysis. The optimal solution was a four-group classification. *Y* axis: composite language scores; *X* axis: time (H0, H24, and D7).

In groups 1 and 4, the aphasia remained unchanged stable over time; the baseline composite language score was low in group 1 (11% of patients) and high in group 4 (29.6% of patients). Baseline composite language scores were high in group 2 (41.8% of patients) and 3 (17.6% of patients); over time, the score decreased gradually in group 2 and sharply in group 3. The trajectory group was significantly associated with presence of a limb motor deficit at baseline ($p < 0.05$); percentages of patients with such deficits were 80, 75, 60, and 95 in groups 1, 2, 3, and 4, respectively. The only other variable that differed significantly across the four groups was the total NIHSS score (not shown). Trajectory modelling using SAS software produced closely similar results (data not shown).

initial low language composite score (group 1), while 29.6% had a high one (group 4); both groups remained stable over time. The remaining patients started out with high scores, some of them showed a sharp decrease (group 3, 17.6% of the patients), whereas the others, the largest group percentage, exhibited a steady decrease (group 2, 41.8%). The relationship between the trajectory group membership and limb motor deficit at admission was statistically significant ($p = 0.0045$), limb motor deficit existing in, respectively, 80%, 75%, 60%, and 95% of groups 1, 2, 3, and 4. There was no statistically significant difference between the four groups for the other variables except for total NIHSS score (not shown).

Discussion

We studied the early recovery of aphasia after thrombolysis in 137 consecutive patients with stroke-related aphasia. The aphasia improved in most patients within 1 week after the stroke and showed a dramatic recovery in 35 patients. Aphasia recovery was significantly better in patients without limb motor deficits. In the 109 patients with both aphasia and limb motor deficits, early improvements in these two impairments were similar in terms of magnitude and timing.

The main strength of our study is the large sample size achieving by recruiting patients at two centres. In addition, we used not only conventional statistical methods but also trajectory modelling to assess changes over time. To obtain a global picture of language capabilities, we created a composite language score by summing NIHSS items 9, 1b, and 1c. Although items 1b and 1c are not specifically designed to test language, the information they provide is important to determine whether aphasia is present. In item 1b, the patient is orally asked the month and his/her age. Trained clinicians can distinguish voice and speech impairments due to dysarthria from symptoms of aphasia. Similarly, apraxia of speech can be recognised based on typical symptoms such as abnormal oro-facial movements. In item 1c, the patient is instructed to open and close the eyes and then to grip and release the hand. This test is sensitive to the presence of motor apraxia but is affected by impairments in oral comprehension (Woo et al., 1999). If the patient does not respond to the command, the examiner should perform the required movements and ask the patient to copy them, in order to detect motor apraxia. Patients with aphasia who do not understand the questions in items 1b and 1c received a score of 2 on both items.

In our cohort of consecutive patients with stroke treated with thrombolysis, the prevalence of aphasia was 40% versus 15–40% in earlier studies (Croquelois & Bogousslavsky, 2011; Engelter et al., 2006; Inatomi et al., 2008; Laska et al., 2001; Maas et al., 2012; Pedersen et al., 1995; Wade, Hewer, David, & Enderby, 1986). As expected, aphasia was almost always due to left MCA infarctions. The small number of cases associated with right MCA occurred in patients who acquired French as a second language late in life or had incomplete right-handedness. The 5.8% prevalence of crossed aphasia in our cohort is slightly higher than the prevalence of 0.4–3.5% reported earlier. This difference may be ascribable to the very early evaluation in our study, as crossed aphasia tends to recover rapidly (Alexander & Annett, 1996; Carr, Jacobson, & Boller, 1981; Croquelois, Wintermark, Reichhart, Meuli, & Bogousslavsky, 2003; Joanette, Puel, Nespoulous, Rascol, & Lecours, 1982; Pedersen et al., 2004).

Aphasia recovery after thrombolysis was better in patients without concomitant limb motor deficits. Few studies have focussed on aphasia recovery in patients with stroke. Inatomi et al. used the NIHSS to evaluate 130 consecutive patients with aphasia, who represented 15.2% of a cohort of 855 consecutive patients with stroke. Thrombolysis was not used. By day 10, among survivors, 46.3% had improved and 20.7% had recovered normal speech, whereas 8.3% had worsened. No predictors of early improvement were identified, and the authors emphasised the difficulty in predicting aphasia outcomes within the first few days following stroke onset (Inatomi et al., 2008). Kremer et al. reported early outcomes of aphasia following thrombolysis in 50 patients (Kremer et al., 2013). At H24, 32% had improved, 62% remained unchanged, and 6% had worsened (Kremer et al., 2013). Of our 137 patients with aphasia, 62.0% had improved by H24, 30.0% had no change, and 11% had worsened. By D7, 81.1% had improved including 32.1% with full aphasia recovery. Felberg et al. reported dramatic recovery during intravenous thrombolysis in 22% of patients who had MCA infarction, with a characteristic pattern of slower and poorer recovery of aphasia compared to limb motor deficits (Felberg et al., 2002). However, only seven patients with dramatic recovery had aphasia, including two with full aphasia recovery, four partial recovery, and one no change. The proportion of patients with full aphasia recovery was similar to that in our group of 35 patients with aphasia and dramatic recovery (2/7, 28% versus 7/35, 20% in our study). Finally, Mikulik et al.

reported the effects within 24 hr of intravenous thrombolysis combined with transcranial ultrasound (CLOTBUST trial) in 113 patients with MCA infarctions (Mikulik et al., 2010). All NIHSS items contributed to the decrease in the total NIHSS score, although to varying degrees. Aphasia responded less well than did the other impairments.

Strictly isolated aphasia was very rare in our cohort of stroke patients (1/338), whereas aphasia without limb motor deficits but with other impairments (e.g., sensory loss, ataxia, or neglect) occurred in about one fifth of patients. After thrombolysis, improvements in aphasia were more marked and occurred more rapidly in patients without limb motor deficits. Whether thrombolysis should be used in stroke patients with aphasia and a low NIHSS score is debated. Aphasia related to mild stroke may have an excellent prognosis. One study found improvement in 57% and resolution in 38% of patients after a median of 5 days after the stroke (Maas et al., 2012). Overall improvement occurred in 86% of patients, and among patients with baseline NIHSS scores lower than 5, i.e., mild stroke, 90% experienced resolution of their aphasia within 6 months. The authors concluded that "the net benefit of thrombolysis in such cases is uncertain." One weakness of this study is the substantial number of patients lost to follow-up (Maas et al., 2012). An interesting point is whether differences in comorbidities exist and explain differences in aphasia recovery. Nesi et al. (2014) recently reported a study of 128 consecutive stroke patients with baseline NIHSS scores ≤6, among whom 47 received intravenous thrombolysis (Nesi et al., 2014). The proportions of patients with unfavourable outcomes after 3 months were 12.8% in the group treated with thrombolysis and 17.3% in the untreated group. Aphasia at the early assessment was the only independent predictor of an unfavourable outcome. The authors concluded that aphasia might warrant thrombolysis even in patients with low NIHSS scores. Our trajectory model identified four groups of patients based on the time-course of the composite language score. Thrombolysis was not followed by any major change in the group characterised by mild aphasia at baseline (group 1). However, these patients had little or no aphasia at discharge, which may be considered a substantial benefit of treatment. The composite language score also failed to improve after thrombolysis in one of the groups with severe baseline impairments (group 4); longer follow-ups are needed to determine whether language improves slowly in this group.

Our study has several limitations. We did not determine the modified Rankin Scale score after 3 months. However, changes between D7 and 3 months in stroke-related symptoms, most notably aphasia, can be affected by numerous factors including environmental influences and depression. The NIHSS on D7 reflects the impact of care in the controlled environment of the hospital. It was suggested recently that the NIHSS score on D7 might be a better end point for randomised trials than the NIHSS score at 3 months or the modified Rankin Scale score on D30 or at 3 months (Kerr, Fulton, Lees, & VISTA Collaborators, 2012). Another limitation of our study is the use of the NIHSS score to detect aphasia and to evaluate aphasia severity. A specific aphasia scale such as the Language Screening Test (LAST) would have been preferable, but this scale had not yet been validated at the beginning of our study. The LAST has two equivalent versions to avoid retest bias. It assesses naming, repetition, automatic sequence, picture recognition, and auditory commands. The total score can range from 0 to 15, and only 2 min is required to administer the test (Flamand-Roze et al., 2011). The LAST is useful for assessing benefits from SLT. SLT can affect the reorganisation of language capabilities and should be offered daily as soon as possible (Godecke, Hird, Lalor, Rai, & Phillips, 2012). SLT seems useful not only to improve language recovery but also to reassure patients and families by providing advice about communication and clues for compensation. Randomised studies are needed to determine the optimal modalities, timing, and intensity of SLT in patients with acute stroke. Our group-based trajectory model identified four groups of patients with aphasia who exhibited different responses to thrombolysis. Clinical characterisation of these four groups might allow increased intensity of SLT in the subgroups at greater risk for a poor response to thrombolysis, and the effects of this strategy would then need to be determined. At both of the study centres, patients received daily speech therapy when appropriate. Future studies of aphasia and its outcomes after thrombolysis should include evaluations with specific aphasia scales, such as LAST, together with tools to assess quality of life, depression, and disability. A study of aphasia comparing patients managed with thrombolysis to controls with mild stroke not managed with thrombolysis might shed light on the current debate about patient selection for thrombolysis (Köhrmann et al., 2009; Kremer et al., 2013; Nesi et al., 2014).

Aphasia not only causes functional disability but also impairs quality of life. Language disorders are probably underestimated at the very early stage of acute stroke. Our study in a large sample shows that aphasia recovery is significantly better in patients without limb motor deficits. A specific language-screening tool, such as LAST, may represent a useful complement to global stroke scales such as the NIHSS for the initial evaluation of patients with stroke and may help to select patients for thrombolysis.

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Conclusion :

Les troubles du langage et les troubles moteurs présentent une évolution similaire dans la première semaine suivant la thrombolyse quand les deux déficits sont associés chez le même patient. Pour une gravité initiale identique, l'aphasie isolée évolue plus favorablement que quand elle est associée à un trouble moteur.

Exploitation, valorisation et diffusion des résultats :

Etude publiée dans la revue **Aphasiology (Impact factor : 1.7)**

Présentation lors de congrès :

Aphasie et troubles moteurs dans les AVC : quelle évolution précoce en suite de thrombolyse ?
C. Flamand-Roze, L. Bayon De La Tour, M. Sarov, J. Yeung, B. Falissard, F. Picot, C. Denier
(Communication affichée. Journées de neurologie de langue française, 2014.)

Conclusion :

Ces années de pratique clinique et de recherche m'ont permis contribuer à apporter des réponses à plusieurs questions scientifiques, et sont également à l'origine de nouvelles interrogations et projets.

1) **La détection précoce des troubles du langage à la phase aiguë des accidents vasculaires cérébraux afin d'améliorer leur prise en charge.**

La détection très précoce des aphasie en phase aiguë des AVC est un facteur favorisant pour la mise en place rapide et adaptée d'une rééducation. Identifier la présence du trouble du langage et le caractériser va permettre une prise en charge adaptée au patient et à sa pathologie propre. En effet, une prise en charge orthophonique des patients avec aphasie, suite à un AVC, est recommandée (25,26,27), même si les résultats des études sont contradictoires dans la littérature. Ces résultats hétérogènes sont probablement le fait d'outils de mesure inadaptés, de cohortes de patients très hétérogènes, de délais de prise en charge variés, et/ou de techniques de rééducation différentes (26,27). La récupération des fonctions du langage associe nécessairement une rééducation adaptée (en fonction de la localisation lésionnelle, de la taille de la lésion, des capacités résiduelles) et la réorganisation neuronale.

Celle-ci mets en jeu la plasticité cérébrale du patient (28). A la suite d'un AVC hémisphérique gauche, la réorganisation fonctionnelle du langage des patients aphasiques impliquerait des interactions intra-hémisphériques entre les aires lésées et les zones péri-lésionnelles mais également des interactions inter-hémisphériques transcalleuses entre l'hémisphère gauche lésé et les régions homotopiques (symétriques controlatérales) de l'hémisphère droit (29). Dans le cas d'une lésion très focale, les aires péri-lésionnelles sont impliquées dans la récupération, en phase aiguë comme lors de la rééducation en phase chronique. Ces modifications à court terme des capacités de langage seraient dues à une hypo-perfusion transitoire de territoires apparemment préservés (pénombre ischémique), ainsi qu'à la réorganisation neuronale précoce (30). Dans le cas de lésions étendues, il semble que la prise en charge du langage se fasse alors par l'hémisphère mineur (31). Cette implication de l'hémisphère mineur a été démontrée par plusieurs études de neuro-imagerie fonctionnelle (32), ainsi que par des études neurophysiologiques en stimulation magnétique transcrânienne (33). L'hémisphère droit peut prendre en charge les fonctions de langage, grâce aux aires homotopiques. Les régions hémisphériques droites les plus aptes à jouer un rôle dans le processus de récupération sont le lobe temporal supérieur (contrôle auditif), les régions pré -motrices et le gyrus frontal inféro-postérieur (planification et séquençage des actions motrices) et le cortex moteur primaire (exécution des actions motrices verbales) (34).

Notre étude sur les aphasies dans les AVC jonctionnels a montré qu'un type particulier de lésion était à l'origine d'une aphasie bien précise. Identifier précocement ce type d'aphasie permet de débuter au plus vite une rééducation adapté. Nous avons pu constater que cette prise en charge précoce et intensive avait débouché sur une normalisation du langage pour nos 8 patients. La récupération du langage est donc probablement due à la combinaison d'une rééducation précoce adaptée et d'une réorganisation neuronale.

Dans le cadre de cette détection précoce, l'échelle LAST est un véritable atout, puisqu'elle permet d'identifier en moins de deux minutes la présence d'un trouble phasique. Grâce à cette détection précoce et rapide, plusieurs patients ont pu bénéficier du traitement par thrombolyse, et la rééducation a pu être initiée rapidement, quelque soit le niveau de gravité du handicap langagier : en effet, les aphasies « légères » à « modérées » peuvent passer inaperçues comparativement aux troubles moteurs plus faciles à détecter. De nombreux patients risquent alors de ne pas être diagnostiqués et de ne pas bénéficier d'une prise ne charge, pourtant nécessaire. De plus, comme nous l'avons constaté dans notre étude sur l'évolution du langage chez les patients thrombolysés, LAST permet d'apporter des informations capitales sur l'évolution du langage en phase aiguë de l'AVC. Ces informations peuvent guider le type de prise en charge, toujours en s'adaptant à la localisation lésionnelle.

2) Vers une nouvelle classification des aphasies ?

Depuis le 19ème siècle, les aphasies ont été classées et décrites selon le modèle connexionniste de neuro-anatomie fonctionnelle du langage établi par Lichtheim en 1885 (35). D'après ce modèle, il existe des régions dédiées à certaines fonctions du langage, comme les aires de Broca et de Wernicke.

Il se présente sous forme d'un schéma et met en jeu 3 régions : l'aire de Broca (M) lieu de l'élaboration (motrice) du langage, l'aire de Wernicke (A) lieu de décodage du langage et un centre (B) non localisable permettant la compréhension du langage et la formulation d'une pensée, relié aux deux régions précédentes. Le fonctionnement du langage repose sur les connexions entre ces différentes régions, d'où le terme « connexionniste » faisant référence à cette approche. En découle les différents types d'aphasie :

- Lésion de A : aphasie de Wernicke ou sensorielle caractérisée par des troubles de la compréhension et de la répétition, un discours fluent voire logorrhéique sans trouble articulatoire, avec un manque du mot et des paraphasies, pouvant aller jusqu'au jargon.

- Lésion de M : aphasie de Broca ou motrice caractérisée par une compréhension majoritairement préservée, un discours non fluent avec troubles de l'élaboration syntaxique, un manque du mot, une répétition altérée et des troubles articulatoires.

- Lésion de 3 (connexion entre A et M) : aphasie de conduction avec altération de la répétition et paraphasies phonémiques, sans trouble de la compréhension ou arthriques.

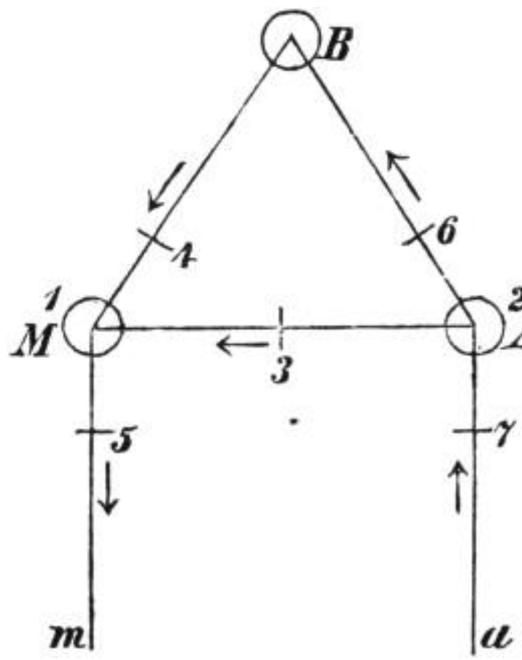
- Lésion de 4 (connexion entre B et A, association des régions auditives et de la compréhension) : aphasie transcorticale sensorielle avec un discours fluent, riche en paraphasies, une répétition préservée. Il existe un trouble de la compréhension associé.

- Lésion de 5 (connexion entre B et M, association de la compréhension et l'élaboration du langage) : aphasie transcorticale motrice caractérisée par un discours non fluent sans troubles arthriques, la compréhension et la répétition étant préservées.

- L'aphasie globale : absence de discours et troubles importants de compréhension serait liée à une lésion de A et M.

- Les lésions de 6 et 7 entraînent des aphasies sous-corticales respectivement la surdité verbale (décodage auditif du langage impossible) et l'anarthrie pure (affection de la réalisation articulatoire du langage).

Schéma « maison » de Lichtheim :



M : aire de Broca ; A : aire de Wernicke, m et a : projections sous-corticale de M et A; B : centre permettant la compréhension du langage et la formulation d'une pensée; 1 à 7 : différents types d'aphasies en fonction de la localisation de la lésion.

1ère limite : Exclusion de certaines aphasies :

Une première limite_de ce modèle est qu'il exclut certaines aphasies, comme l'aphasie par manque du mot isolé ou aphasie anomique ainsi que les troubles du langage écrit (alexie/agraphie acquise).

2ème limite : non prise en compte de la variabilité dans le temps et inter-individuelle

Le langage implique de nombreux réseaux qui constituent un ensemble fonctionnel. Il existe une plasticité cérébrale dont il faut tenir compte lors du raisonnement neuro-anatomique. Il en découle une certaine variabilité clinique : pour une localisation donnée selon la nature de la lésion et chez un même patient au cours du temps. Kreisler et al. (36) a montré des résultats sur 107 patients qui s'accordaient avec la classification connexionniste. Cependant, cette étude a été réalisée dans les 4 semaines suivant l'AVC. Ce délai pose un problème méthodologique majeur, compte tenu de l'évolution rapide des troubles phasiques dans les dix jours qui suivent l'AVC. L'aphasie évolue donc rapidement d'un type vers un autre. De plus, on sait que l'organisation du langage est variable d'un individu à un autre, en fonction de son histoire, de son apprentissage de langues étrangères, et de sa latéralité.

3ème limite : non prise en compte des réseaux.

Une troisième limitation de ce modèle est l'hypothèse que les fonctions des aires sont fixes et limitées. Les moyens d'investigation comme l'IRM (Imagerie de Résonance Magnétique) ou l'EEG (électroencéphalographie) ont permis de mettre en évidence de nouvelles interactions inter et intra hémisphériques, allant au delà des aires de langage classiques. La découverte de nouvelles régions d'activité a permis de créer de nouveaux modèles, comme le modèle dorsal/ventral (37) ou le modèle des réseaux frontaux, qui prennent en compte les fonctions non linguistiques : d'après Carpenter, l'organisation corticale des fonctions exécutives et de la mémoire de travail est distribuée au delà des régions pré-frontales. Il est donc difficile d'identifier des mécanismes spécifiques à une région neuronale. En effet, on peut maintenant affirmer qu'il existe une interaction constante entre langage et attention, mémoire, praxies, fonctions visuo-spatiales et affectivité.

En 2012, Poeppel (38) affirme que l'ancien modèle doit être repensé, grâce à ces nouvelles techniques d'imagerie qui ont permis de créer une nouvelle cartographie de l'anatomie fonctionnelle du langage. Une région anatomique sous-tend plusieurs fonctions, et est séparée en sous régions (environ 10). Cette nouvelle approche, par les réseaux, permet de ne pas limiter le langage à l'hémisphère gauche et aux fonctions d'expression et de compréhension.

Un outil comme LAST, validé en phase très aiguë de l'AVC, pourrait permettre de travailler sur un nouveau modèle de fonctionnement en réseaux. En effet, LAST permet de détecter les fonctions du langage altérées. Une étude portant sur un grand nombre de patients et se basant sur les résultats à LAST pourrait déterminer des liens entre les IRM, scores aux différents subtests, et évolution très précoce.

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